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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 21 1955

CLASSIFICATION OF THE EPILEPSIES*

BY

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No lecture on epilepsy can begin without reference to Hughlings Jackson, who almost a century ago defined epileptic seizures as the expression of occasional, sudden, excessive, rapid, local discharge in the grey matter. This definition needs hardly any qualification to-day. Yet within the last fifteen years our knowledge of epilepsy has greatly expanded owing to the introduction of the electroencephalogram, a method by which the discharge, which was for Jackson hypothetical, can now be seen and recorded in many seizures. The knowledge thus gained is still in process of assimilation, and what we believe to-day may no longer be true in a year's time. I am not perturbed by this reflection. It is necessary for clear thinking to have beliefs. It is equally important that we should be prepared to change them, which is not so easy. I would commend to you in this connexion Sir Thomas Browne's saying that "to purchase a clear and warrantable body of truth, we must forget, and part with, much of what we know."

If we are to think clearly about epilepsy we must begin by arranging our observations in some kind of order. The classification of seizures in terms of medical science is in itself a problem which has exercised many minds in recent years. I shall put before you the method of classification which I have proposed myself and believe at present to be the most satisfactory. It requires tabulation of the data under separate headings, and the most convenient arrangement is in parallel vertical columns.

The first heading is Clinical. A seizure is a clinical event, and the symptoms observed, or elicited by questioning the patient, must be classified in terms of clinical usage. What these terms should be I will discuss later. It will suffice for the moment if I say that under the Clinical heading we shall record clinical phenomena only—for example, loss of consciousness, convulsive movements, odd behaviour, and abnormal sensations. The heading for the second column is Anatomical. If we accept Hughlings Jackson's definition—and there is no reason to doubt it—the discharge must begin somewhere in the brain. It will be our aim under this heading to indicate the site of origin of the discharge. The third heading is Physiological. Seizures may be accompanied by observed disorder of function in the neurones. Of this the only example at present known is the physical disturbance recorded by the E.E.G.

The fourth column is Pathological. The terms of classification in this column will be those to which we are all accustomed, inflammation, trauma, new growth, and so on. Finally, I think it useful for practical purposes to have a column in which to record any specific response of seizures to particular drugs or other forms of treatment. A convenient heading will be Therapeutic. In this column we shall make such entries as dione-responsive, primidone ("mysoline")-responsive, and so on. Our object, of course, will be to establish correlations between groups of data in the different columns.

*A clinical lecture delivered at Guy's Hospital.

Clinical Patterns of Seizure

I will now go back to consider the classification of seizures in clinical terms. The simplest method is to make use of the plan followed in recording a neurological examination. We begin with the mental state and record loss or clouding of consciousness, disordered behaviour, disturbance of thought, hallucinations, and illusions. Next comes speech, which may be arrested or disorganized in a seizure. After this we take the special senses, any of which may be involved in an attack. Then we have the motor system to consider, which will include a large part of our clinical data—convulsive movement, tonic or clonic, generalized or localized. Sensation will also include many data provided by the patient's account of numbness, tingling, and other somatic sensory experience in attacks. Finally, there is the important heading for visceral symptoms, which may be motor—for example, vasoconstriction, salivation, or involuntary micturition—or sensory—for example, the well-known epigastric aura. The visceral symptoms are commonly both motor and sensory.

I shall not attempt to describe the great variety of symptoms or combinations of symptoms that may be observed in epileptic seizures. The point I wish to make now is that it has been possible to relate certain clinical patterns of seizure to certain anatomical sites of discharge, so that we can speak of pre-central or post-central seizures, temporal-lobe seizures, occipital-lobe seizures, and so on.

In this process of clinico-anatomical correlation the E.E.G. has proved very useful, for when the epileptic discharge arises near the surface of the brain it is associated with a localized electrical disturbance which can often be recorded, either in association with seizures or in the intervals between them. This is a more delicate, and often a more certain, method of establishing the site of the discharging lesion than any other, and has made us more confident of the relationship between clinical pattern and anatomical site than when we had to depend upon the evidence provided by pathological lesions. Sometimes the E.E.G. will indicate the site of discharge when the clinical pattern is of doubtful value. On the other hand, the clinical pattern may sometimes be distinctive when the E.E.G. fails to reveal any localized discharge, probably because the discharge is arising deeply and is therefore not picked up by the scalp electrodes.

Contribution of the E.E.G.

Apart from its localizing value, the E.E.G. may sometimes provide data for use in the pathological column. For example, replacement of the normal alpha rhythm by localized very slow wave activity indicates an active or recent destructive lesion. Generalized slow-wave activity is met with in the presence of increased intracranial pressure.

But the main contribution of the E.E.G. to the study of epilepsy has arisen from the discovery that there is a large group of seizures associated with a particular *pattern* of electrical disturbance. In this instance the data belong to the physiological column. The distinctive feature of this pattern of discharge is that it is bilateral, synchronous, and symmetrical. Now, taking the physiological column as our point of departure, we may proceed to see what correlations can be established with data in the other columns. The clinical pattern of seizures associated with this type of E.E.G. is quite simply described, but at this point we must digress for a moment to define terms commonly, and sometimes loosely, used in the clinical description of seizures—major or grand mal, and minor or petit mal. It is generally accepted that a major seizure is one in which there is loss of consciousness and generalized convulsive movement. Any other kind of seizure is usually described as minor epilepsy. This division is, I think, unsatisfactory, for there is a great variation, not only in the pattern but in the duration of seizures which would thus be included in the minor category. I can see no completely satisfactory solution for this difficulty, but if we take as our measure the *duration* of the attack we shall find that there is a large group in which the seizure is over in less than a minute. As a term of clinical usage petit mal was often in the past employed to describe these very brief seizures, but, as I shall later explain, petit mal has now lost its purely clinical meaning. It is convenient to have a term for these little attacks, and minimal seizure is, I think, appropriate, provided that we remember that the word "minimal" refers only to the duration of the seizure.

Now, when we examine the clinical features of attacks associated with the bilateral, synchronous, and symmetrical discharge we find that they are either minimal seizures of a particular kind or major seizures which from the moment of onset are attended by loss of consciousness and generalized convulsion. I must reiterate that these major seizures are not preceded by any other symptoms. As we shall observe later, an epileptic discharge arising in any part of the brain can spread to involve the whole of it and will then be attended by loss of consciousness and generalized convulsion. In such attacks—focal or partial seizures—there is nearly always some initial symptom corresponding with the site of the initial discharge, and if the onset of an attack can be recorded by the E.E.G. localized discharge will be apparent, preceding the general spread. But in the seizures of the group which we are now discussing both the convulsive movements and the electrical discharge are symmetrical and generalized from the first.

Minimal Seizures

The minimal seizures of this group are of two kinds, each as a rule well defined. The most frequent form is the "lapse" or "absence." There is a sudden, brief suspension of mental function with loss of consciousness. The whole episode lasts from 5 to 15 seconds, and may easily pass unnoticed. During the attack the patient has a fixed stare and is motionless, but there is sometimes twitching of the eyelids and occasionally of the arms, and the eyeballs may turn upwards. The seizure ends as abruptly as it began, and the patient will continue with what he was previously doing or saying as if there had been no interruption. Sometimes the lapse may be longer and last up to a minute, but it is probable that in such cases there has been a very rapid succession of brief attacks. Occasionally the lapse may be incomplete—that is to say, consciousness is not lost, but clouded, and the patient may be able to describe a momentary state in which he is dimly aware of what is going on around him but unable to initiate thought or action. But where consciousness is lost—and this is the general rule—he has no memory of the time during which the seizure occurred, being aware of the interruption only when it is over.

The other form of minimal seizure observed in patients of this group is the myoclonic attack. This consists of involuntary jerks of the muscles without loss of consciousness. These jerks are usually bilateral and symmetrical, but vary in their extent and distribution. They are often confined to the upper limbs. The duration of the jerks is very brief, not more than a fraction of a second, but there may be a succession or volley of jerks. If the jerk is of large extent whatever is held in the hand may be flung into the air, or if the trunk and lower limbs are involved the patient may be thrown to the ground. Occasionally there may be loss or clouding of consciousness in a myoclonic seizure, but as a rule the patient is aware of all that is happening.

A third variety of minimal seizure has been described as belonging to the group under consideration—the so-called "akinetic" attack in which the patient falls, without loss of consciousness and without myoclonus. Doubt has been cast upon this interpretation, the alternative explanation being that the fall is due to a brief single myoclonus involving the lower limbs. Of this it is difficult to be certain, but I believe from my own observation that true akinetic seizures do occur, and this belief is supported by accounts given by intelligent patients who describe their minimal seizures as of three separate kinds—"blanks," "jerks," and "falls."

Differences in E.E.G. Wave Form

This, then, briefly is the clinical range of attacks associated with the bilateral, synchronous, symmetrical abnormality in the E.E.G.: major seizures of the generalized type, and two, or possibly three, species of minimal seizure. Corresponding with these different types of seizure there are differences in the wave form of the E.E.G. In the major seizure the normal alpha rhythm is replaced by waves of a much higher voltage, though of about the same rate—10 cycles per second—giving rise to a series of spikes, which continues unaltered throughout the tonic phase of the convulsion. In the clonic phase the series of spikes is interrupted by rhythmic slow waves corresponding with the intervals between the clonic spasms. In the form of minimal seizure represented clinically by a lapse of consciousness, the E.E.G. shows a regular sequence of alternating spikes and slow waves at a fairly constant rate of three spike-and-wave complexes per second. The myoclonic jerks are associated with isolated spikes or short runs of spikes which may be mixed up with an occasional slow wave. The akinetic seizure, whose existence is now doubted by some authorities, is accompanied by an E.E.G. of the same type as that seen in myoclonic seizures.

Anatomy and Pathology

We have now established in some detail correlations between physiological and clinical data for this group of seizures and must proceed to examine the data in the other columns. The anatomical site of discharge as determined by the E.E.G. would appear to be generalized, but it seems probable from animal experiments that bilateral, synchronous, symmetrical discharge in the cerebral cortex may represent the effect of an initial discharge arising in the central grey matter and propagated to the cortex. The evidence for this is strong enough to have given rise to the term "centrencephalic," or more simply central epilepsy, for this group of seizures, so that we may provisionally enter the word central under the anatomical heading.

Under the pathological heading there are no positive data to record, for no one has ever been able to discover any histological basis for this group of seizures, which therefore remains idiopathic in the traditional sense of that word.

We may therefore enter the word idiopathic under the pathological heading. Incidentally it is in this group of seizures that heredity seems to be of more importance than in any other, so that we might perhaps add genetic in brackets under idiopathic.

Therapeutic Data

There now remains the therapeutic column, and in this we have important data to record, for the minimal seizures of this group often respond in dramatic fashion to the dione group of drugs, of which troxidone ("tridione") is that generally used. Dione-responsiveness appears to be specific for this particular type of seizure. It has no beneficial effect upon the major seizures of this group and may even increase their frequency. On the other hand, the drugs which are often effective in controlling the major seizures have usually no effect upon the minimal seizures.

To summarize the data we have now recorded for this group of seizures, they are as follows :

Clinical	Anatomical	Physiological	Pathological	Therapeutic
1. Major—generalized	Central	Bilateral, synchronous, symmetrical E.E.G. discharge	Idiopathic (genetic)	—
2. Minimal (*a*) lapses (*b*) jerks ..				Dione-responsive

"Central Epilepsy"

We now need a single descriptive term for this group of seizures. So far as the E.E.G. is a guide, the discharge being generalized, we might use the term "generalized epilepsy." Or we might speak of "central epilepsy" or of "idiopathic epilepsy," and in fact all these terms have been, and still are, used. This, I suppose, does not matter so long as we all understand what is meant. For myself, I prefer the term "central epilepsy," because it is a new one and therefore less liable to misinterpretation than terms which have been used in the past in other ways.

There are, however, some further problems of nomenclature which must be discussed if we are to understand what is being written about the epilepsies. You will find that petit mal is now generally used in a specific way to denote minimal seizures of the central type. Sometimes they are called true petit mal, with the implication that, although minimal seizures of similar clinical appearance may occur in association with other forms of E.E.G., it is only those minimal seizures having the bilateral synchronous patterns of E.E.G. that should truly be described as petit mal. The use of the name petit mal in this sense has been widely accepted, and I have no objection to it so long as it is remembered that it is a definition in terms of the E.E.G. and not a term of clinical description.

If we are going to call the minimal seizures of central epilepsy petit mal, it would seem quite logical to call the major seizures grand mal, again remembering that the E.E.G. is the criterion, and using grand mal only to describe major seizures of the central type. Having thus defined central epilepsy with its subdivision into petit mal and grand mal, I must deal very briefly with the natural history of the disease.

Petit mal seizures nearly always begin in childhood, and from the first occur with great frequency, up to 20 to 30 times a day. They are sometimes controlled by troxidone, but even if they are not they may cease about the age of puberty, never to recur. The lapses are so brief that they need not as a rule interfere with normal education, and the same is true of the jerks, unless they are so extensive as to cause falling. In a considerable proportion of the cases, however, the petit mal seizures are followed sooner or later by grand mal, and the liability to seizures of this type is likely to persist, with or without continuation of the petit mal. A series of myoclonic jerks during the first hour after waking in the morning is especially apt to conclude with a generalized convulsive seizure.

Grand mal seizures, with or without petit mal, may begin at any age, but rarely after 30. The drugs which have proved most effective in the treatment of grand mal are phenobarbitone and phenytoin sodium in combination, primidone, and methoin. The principles of treatment are simple. The drug or drugs chosen should be given first in moderate dosage. If the attacks continue, the dosage should be gradually increased up to the point at which either the attacks cease or intolerable toxic symptoms occur. In the latter case another drug or combination of drugs should be tried in the same way. Each therapeutic trial should be continued long enough for a just appraisement of the effect, having regard to the frequency of seizures before treatment was started. In this way the best medication can be determined, and in a considerable number of cases the seizures, even if they are not abolished, can be brought down to a frequency which is not incapacitating.

"Partial Epilepsy"

In all forms of epilepsy other than that which I have defined as central epilepsy, the clinical and E.E.G. data indicate a discharge arising in some part of the brain. It may be restricted to this part or spread to other parts, but the initial discharge is localized. This is what in the past has been called focal epilepsy, but Gastaut (1954), whose recent monograph, *The Epilepsies*, I would commend to you, prefers the term partial epilepsy for good reasons. It was for a long time supposed that focal epileptic seizures always arose from cells in the cortex and that there was a specific relationship between a particular cortical focus and a particular pattern of seizure. This no longer appears true, the fact being that the cortical neurones represent only one link in a circuit comprising at a deeper level neurones of the central grey matter. Cerebral function is represented not in a cortical mosaic but in sectors of brain which include cortex, optic thalamus (and other basal ganglia), and connecting neurones. The discharge responsible for a partial (as opposed to a generalized) seizure may arise either in the cortical or in the central grey matter. Partial epilepsy, proposed by Gastaut instead of focal epilepsy, is therefore a better term, and I think it should be adopted.

Of the symptoms of partial epilepsy there is an endless variety. I have been especially interested in the clinical patterns of seizures all my clinical life and continue to learn new ones. Hughlings Jackson penetrated to the core of the matter when he said 75 years ago that there were as many different epilepsies as there were sites of discharging lesions. Partial seizures may be of the major, minor, or minimal degree, depending upon the amount of spread of the discharge. In the major seizures there may be little or no clinical evidence of a localized onset, though careful questioning of the patient or a witness of the attack will often bring some important point to light, as, for example, twisting of the head and eyes to one side before the onset of generalized tonic spasm, or the memory of an unpleasant smell or visual hallucination before consciousness was lost. The minor or minimal seizures are much richer in clinical clues, for consciousness is often preserved, or is lost relatively late in the attack, and the patient is able to give an account of the initial symptom. Many partial seizures are thus easily identified—pre- and post-central from localized spasm or sensory disturbance, occipital from crude visual hallucinations, postero-inferior frontal from adversive movement of head and eyes, and some of the temporal lobe seizures from the occurrence of an olfactory aura, masticatory movements, or a dreamy state.

Murray Falconer (1954) has given an excellent account of the many seizure patterns that may result from discharge in different parts of the temporal lobe region. But discharge arising in this region or in the frontal lobe may begin and end with loss of consciousness. It may therefore be very difficult, sometimes I think impossible, to distinguish clinically between a minimal seizure arising from

the frontal or temporal regions and the lapse of petit mal, and here the E.E.G. may be of critical importance in arriving at a correct diagnosis.

You will have observed that I have attached a good deal of importance to the E.E.G. in distinguishing between central and partial seizures and in the localization of the site of discharge in the latter, but, as I have already indicated, the E.E.G. is by no means infallible. A positive E.E.G. depends first upon the chance of an epileptic discharge occurring while the record is being made. This chance may be a very small one, though various methods are now used to precipitate what are called subclinical seizures while the record is in progress. Nevertheless there are a great many cases in which we can be quite sure from the clinical evidence that the patient is suffering from epilepsy yet the E.E.G. is negative. This may be true for partial seizures even though the patient is having clinical attacks at the time the record is made. We recently had in the wards a man who was having partial seizures of precentral origin with tonic and clonic convulsive spasm involving the left side of the face and adversion of head and eyes to the left. These occurred frequently during the period of the E.E.G. record, which showed no abnormality. It is probable in this case that the discharge was arising deeply.

One of the most interesting developments in recent years has been in our knowledge of the pathology of partial seizures, for which it seems possible that there is always an organic cause to be found—that is to say, a demonstrable histological lesion. The importance of scars, due to birth injury, neonatal anoxia, or encephalitis, has been increasingly revealed from the study of brain substance excised by neurosurgeons. Mr. Murray Falconer's lecture has told of what is now being done in the surgical treatment of partial epilepsy.

Conclusion

I will conclude with a brief account of the steps which should be taken in the investigation of a case of epilepsy. First and foremost there is the clinical history, including, of course, the family history, birth, neonatal symptoms, and past history, with special reference to any head injury, or encephalitis complicating one of the exanthemata, leading up to the description of the seizures, by patient and witness. Next comes the neurological and general examination. When this has been completed the distinction between central and partial epilepsy can very often be made on clinical grounds. It is, however, I think essential to have an E.E.G. in every case, for the combination of clinical and electrical data provides the surest basis for diagnosis and treatment. If the clinical and E.E.G. evidence agree in indicating the diagnosis of central epilepsy there is no need for radiographs of the skull, but in every case of partial epilepsy, or *whenever there is any doubt*, radiographs should be taken. It is true that they will usually reveal nothing, but if this step is not taken the presence of a benign tumour may be missed, at a stage at which there are no symptoms of increased intracranial pressure or any abnormal physical signs—the stage, in fact, at which a benign tumour can be most safely removed. Many benign tumours of the kind which present with epileptic seizures contain areas of calcification; others may cause a shift of the calcified pineal, or erosion or thickening of bone. It has happened to me twice in the last three years to have encountered a patient in the early teens with seizures taking the form of attacks of unconsciousness, sometimes going on to generalized convulsive spasm, with no certain clue to the site of discharge, and without any other symptoms or signs, in which the radiograph revealed a calcified mass in the left temporal lobe. In each instance this proved to be a benign intraventricular tumour, which was successfully removed.

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A NEW TREATMENT OF BARBITURATE INTOXICATION

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The increasing popularity of barbiturates as suicidal agents has created a world-wide problem, and over the past decade the amount of barbiturate used on both sides of the Atlantic has more than trebled, while the incidence of barbiturate coma has increased fivefold (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954; Goldstein, 1947; Koppanyi and Fazekas, 1950, 1952, 1954; Møller, 1954; *Lancet*, 1951, 1953; Goodman and Gilman, 1947). Until recently the over-all death rate from barbiturate intoxication treated with central analeptics of different types has remained steady at about 10%, increasing to over 20% in serious cases (defined by Nilsson as " one which has been in coma for 24 hours or in which complications are present "). This figure has now been reduced as a result of improved medical care (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954) and possibly, although to a much less extent, the more judicious use of the newer central analeptics (Koppanyi and Fazekas, 1950, 1954; Eckenhoff *et al.*, 1949). We wish to discuss a new method of treatment incorporating the use of two new substances, $\beta\beta$-methylethylglutarimide (NP13) and 2:4-diamino-5-phenylthiazole hydrobromide or hydrochloride (D.A.P.T.), which we feel should, when used in conjunction with good medical treatment, further reduce the death rate from this condition.

In our small series of 41 cases of pure barbiturate intoxication, of which nine were serious, there was one death, which we suggest was not due to the treatment, and we feel that the method has been promising enough to warrant further large-scale clinical trials.

The merit of the method lies in the fact that the more active agent, NP13, unlike the central analeptics in current use, appears to exert, in therapeutic doses at least, a direct antagonism to the offending barbiturate, and will readily restore the patient from a deep coma to a desired state of light anaesthesia—" the safe state "—from which spontaneous recovery to full consciousness usually occurs within eight hours. This removes the need for strict and prolonged medical and nursing care (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954; Møller, 1954) and virtually eliminates the risk of complications. The chemical structure of NP13 indicates a definite resemblance to the barbiturate ring system.

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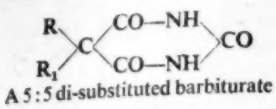
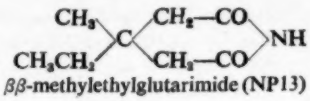
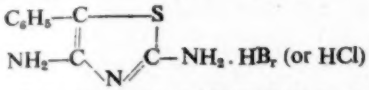


A 5:5 di-substituted barbiturate



ββ-methylethylglutarimide (NP13)



2:4-Diamino-5-phenylthiazole hydrobromide or hydrochloride (D.A.P.T.)

D.A.P.T., itself a weak barbiturate antagonist, is, however, a good synergist to NP13 as well as an excellent respiratory stimulant. It greatly reduces the risk of toxic manifestations, which sometimes occur when NP13 alone is given rapidly and in high dosage. Both substances in therapeutic doses appear to cause a slight rise in blood pressure, and a large dose (75 mg.) given intravenously to a barbiturized patient has produced a large rise in blood pressure and sweating, suggesting a direct effect on the autonomic ganglia. However, both substances, especially NP13, in high dosage, and particularly if given rapidly, will cause convulsions in both barbiturized and normal animals (Benica and Wilson, 1950; Shaw *et al.*, 1954), and we have often deliberately induced convulsions in dogs several times in the course of a single experiment without the loss of an animal. However, full animal investigation (Shaw and Bentley, 1952; Shaw *et al.*, 1954) has indicated that these substances possess a high therapeutic index, and no signs of toxicity have been observed with the suggested method of treatment. Investigation of the mode of excretion of NP13 and estimations of the barbiturate content of the cerebrospinal fluid, blood, and urine of our patients were carried out in collaboration with N. E. W. McCallum, Department of Pathology, University of Melbourne. Preliminary work has shown that much of the NP13 is excreted in the urine unchanged.

Method of Treatment

The treatment suggested for cases of barbiturate intoxication consists of: (1) general medical treatment; and (2) specific treament with NP13 and D.A.P.T.

1. General Medical Treatment

As our patients were returned fairly quickly (two hours) to the "safe state" we have been able to dispense with many of the elaborate procedures employed by Nilsson *et al.* in their prolonged management of the comatose patient. We have found the following minimal procedures satisfactory. A laryngoscope is passed in the casualty department to assess the pharyngeal and laryngeal reflexes. If these are absent a cuffed tube is inserted, and the stomach contents are carefully aspirated if the patient is treated within 4–5 hours of ingesting the barbiturate. Gastric lavage should not be performed (Møller, 1954; *Lancet*, 1951). An antibiotic "cover" should be employed. The patient is then transferred to the ward if necessary and a clear airway and adequate oxygenation are ensured. Close watch should be kept for complications.

2. Specific Treatment with NP13 and D.A.P.T.

This should preferably be given in the ward, and an emergency tray containing, amongst other things, 2.5% thiopentone sodium should be at hand in case the patient should show any idiosyncrasy to these drugs. The two drugs are administered in physiological saline in the following dilutions: NP13 0.5% (5 mg. per ml.) and D.A.P.T. 1.5% (15 mg. per ml.).

Preparation of Solutions.—NP13 is relatively insoluble in water at neutral *p*H and room temperature, and 0.5% approaches the maximum degree of solubility obtaining under these conditions. This low solubility is not a disadvantage, as it minimizes the risk of overdosage. Of the crystalline powder 2.5 g. should be dissolved in 500 ml. of physiological saline at 80°–90° C. The resulting colourless solution is autoclaved and is then ready for use. This solution appears to retain its activity for over three months.

D.A.P.T. decomposes on autoclaving when in solution, but is perfectly stable in the solid state; consequently 300 mg. of the dry sterilized powder is dissolved in 20 ml. of physiological saline as required. The resulting colourless solution is stable at room temperature for up to 24 hours.

Mode of Administration.—Our experience to date has led us to adopt the following procedures:

Set up a 5% glucose intravenous infusion (dextran if indicated) as a means of affording rapid action of the drugs.

Inject, by two separate (20-ml.) syringes, into the rubber tubing of the drip every three to five minutes, 1 ml. D.A.P.T. solution, followed immediately by 10 ml. NP13 solution. This probably allows more control than would direct infusion of the two solutions. Decrease these quantities by half if the patient's response should cause concern. The response is assessed by the following, noted after each injection: Pulse, respirations, blood pressure, tone, reflexes (knee, ankle, plantar withdrawal; the return of laryngeal and pharyngeal reflexes is judged by their effects on the endotracheal tube or, in its absence, by signs of swallowing and coughing); eye signs (movement, lacrimation, reaction of pupil to light); presence of voluntary movement, reaction to supraorbital pain stimulus (often misleading); phonation, state of peripheral circulation, colour and temperature of skin. These afford a good progress report of a patient's recovery.

Continue the injections until the patient is brought to the "safe state," denoted by a return of tone and reflexes (including pharyngeal and laryngeal). This is usually associated with groaning, voluntary movement, and return towards normal of pulse rate, respiratory rate, and blood pressure. The treatment generally takes about two hours in a deeply comatose patient. A total dose of 200 ml. (1.0 g.) NP13 solution and 20 ml. (0.3 g.) D.A.P.T. solution is usually adequate in most cases (see Tables I and II). No attempt should be made to wake the patient.

Once the "safe state" has been reached, remove the endotracheal tube and treat the patient as if recovering from light anaesthesia. Spontaneous recovery to full consciousness usually occurs within eight hours.

Signs of Toxicity

Vomiting or retching is usually the earliest, and may be the only, clinical sign of incipient toxicity. This may rarely be followed by slight flickers of the fingers. In bringing a barbiturized patient to the "safe state" toxic effects are unlikely unless the drugs are given more rapidly or in larger doses than suggested. Should they occur, however, treatment should be temporarily suspended, and, should they be severe, they may be readily reversed by a small intravenous dose of 2.5% thiopentone sodium. A more accurate indication of incipient toxicity is obtainable if the treatment is carried out under electroencephalographic control.

Regression

If after the patient has been brought to the "safe state" his condition regresses, further small treatments may be given as required (Cases 10, 12, 14, 15, 21, 24, 25, 35, 36, 39). Regression is more likely to occur when the coma has lasted a long time before treatment is started, or if the barbiturate concerned is a long-acting one (such as phenobarbitone).

Advantages

The rapid restoration of the comatose patient to the easily manageable "safe state" has three advantages: (1) It obviates the need for prolonged endotracheal intubation; (2) it minimizes both the immediate risk to the patient's life and the remote risk associated with possible complications

of prolonged barbiturate coma; and (3) it is valuable from the viewpoint of hospital economy in that it affords relief from prolonged and strict nursing.

Results of Treatment

Details of illustrative cases are presented in Table I, showing (*a*) the response to treatment with NP13 and D.A.P.T. of a patient suffering from an overdose of a short-acting barbiturate (Case 17); (*b*) the response in a patient with an overdose of a long-acting barbiturate (Case 18); (*c*) the response of a "serious case" (Cases 11 and 24); (*d*) regression (Case 24); and (*e*) the effects of NP13 overdosage (Cases 1 and 26). Table II gives a synopsis of the other cases treated.

The proportion of serious cases in our series (10, 11, 12, 15, 24, 25, 32, 35, 36) was about 25%. Eight patients (Cases 6, 7, 9, 19, 27, 30, 33, 34) presented a picture of light barbiturate coma and would probably have awakened spontaneously without specific therapy, although not nearly so quickly. We found phenobarbitone to be the most frequently ingested barbiturate, with "seconal" (quinalbarbitone), "carbrital" (phenobarbitone+carbromal), and "nembutal" (pentobarbitone) slightly less common. Our oldest patient was 84, the youngest 14. The longest periods of coma preceding treatment were 80 hours (Case 10) and 6 days (Case 32).

Nine patients were treated with NP13 alone (Cases 1–6, 8, 26, 37), and one (Case 33) with D.A.P.T. alone. Signs of overdosage were observed in four of our earliest cases (1, 2, 3, 26), and were due to administration of excessive doses of NP13 in an endeavour to restore complete consciousness immediately. The risk of overdosage was subsequently minimized by using a mixture of NP13 and D.A.P.T. and stopping when the patient had reached the "safe state."

This condition of overdosage, manifested by excessive excitement and restlessness on awaking, was effectively reversed by sedation with paraldehyde or a barbiturate such as quinalbarbitone, amylobarbitone, or diallylbarbitone. No residual effects were encountered.

Thirty patients given a mixture of NP13 and D.A.P.T. (Cases 7, 9–25, 27, 30–32, 34–41) were readily brought to the "safe state," from which they awoke spontaneously, usually within eight hours. No toxic manifestations, either acute or chronic, followed.

Ten patients (Cases 10, 12, 14, 15, 21, 24, 25, 35, 36, 39) regressed and received more than one treatment. This generally followed (*a*) the ingestion of a large dose of barbiturate, usually of the long-acting variety, or (*b*) a long delay before specific treatment was started. In Case 14 the second treatment was purely diagnostic to assess the degree of regression.

The largest effective single dose of NP13 used in one treatment was 2.0 g. (Case 8), and of D.A.P.T. 0.62 g. (Case 12). The largest effective over-all dose of NP13 used in one patient was 5.49 g., and of D.A.P.T. 1.70 g. (Case 24).

The most reliable single sign of a favourable response was the plantar withdrawal reflex, its increased activity usually paralleling the patient's progressive recovery. The fact that NP13 has some analgesic properties of its own made the response to supraorbital pressure an unreliable index of recovery.

Our experience to date indicates that treatment with NP13 and D.A.P.T. is quickly effective in reversing the most severe respiratory and circulatory depression accompanying barbiturate intoxication. Indeed, on restoring the patient to the "safe state" the blood pressure, pulse rate, and respiratory rate usually return towards normal. The respirations, previously shallow, irregular, and sometimes stridulous, assume a deep, regular, and more even character. We have had no occasion to give vasopressor agents once the specific treatment has been instituted, and we feel that these should be

TABLE I.—*Reports of Selected Cases of Barbiturate Intoxication*

Case No.	Age and Sex	Agent and Quantity Taken	Duration of Coma before Treatment (Hours)	State before Specific Treatment	Total Specific Treatment (Dose in Grammes)	Dose (in Grammes) Required to Produce "Safe State"	State after Treatment	Comments
17	F 40	Quinal-barbitone 2 g.	5	P. 120, R. 22, B.P. 140/90. Atonia, areflexia, no response to supra-orbital pressure. Pupils sluggish to light. Moist crepitations in chest	NP13 D.A.P.T. 0·45 0·2 in 1 hour	NP13 D.A.P.T. 0·45 0·2 in 1 hour	P. 80, R. 18, B.P. 170/110. Brisk reflexes, good tone, marked reaction to painful stimulus, voluntary movement of whole body. Responds to orders; asked for a drink of water	No regression. Following morning: Feels well; rational; wants to go home; no signs of toxicity. 3rd day: Tried to walk out of hospital; restrained. 4th day: Signed herself out. Routine tests: Only abnormality low serum potassium (3·6 mEq/l.). E.E.G.: Return to normal pattern, no signs of drug toxicity
18	M 34	Phenobarbitone 3·3 g. +alcohol	7	P. 120, R. 26, B.P. 120/80. Knee reflexes slightly active only. Ankle clonus. Atonia, pupils fixed and unreactive. No response to supra-orbital pressure. Peripheral return poor, rectal temp. 95° F. (35° C.)	1·8 0·57 in 3 hours	1·8 0·57 in 3 hours	P. 132, R. 24, B.P. 125/80. Reflexes brisk, good tone, swallowing, coughing, groaning, trying to get up, obeying orders. Pupils react briskly to light. Colour and peripheral return good	No regression. Quite conscious and trying to get up. Following morning: Talking rationally though a little dull; eating. 3rd day: Well, wants to go home, asks about wife; uneventful recovery. Routine tests: No abnormality detected. E.E.G.: Within normal limits
11	F 36	Butobarbitone 8·3 g.	17	P. 120, R. 6, B.P. 85/60. Cold and cyanosed. Atonia, areflexia, incontinent. Pupils irregular and fixed. No response to supra-orbital pressure. Peripheral circulatory failure	3 doses of 9 mg. picrotoxin given ½-hourly produced transient return of reflexes 1·2 0·44 in 1½ hours	1·2 0·44 in 1½ hours	P. 110, R. 18, B.P. 110/80. Reflexes brisk, groaning, voluntary movement of head and body, good tone, brisk pupillary light reflex	No regression. 6 hours later: Co operative, speaking, obeying orders. 2nd day: Tried to walk out of hospital; restrained. 3rd day: Discharged for psychiatric treatment. Routine tests: Only abnormality low serum potassium (3·3 mEq/l.). E.E.G.: Normal tracing on day of discharge
24	F 47	Phenobarbitone 7 g.	30	P. 80 (weak), R. 10, B.P. 50 ?. Areflexia, atonia, fixed pupils. No response to supraorbital pressure. Cyanosed, peripheral circulatory failure, chemotic conjunctivae	(1) 0·9 0·15 in 2 hours	0·9 0·15 in 2 hours	P. 90, R. 32, B.P. 95/60. Some reflexes present. Patient spastic. Respirations good depth and regular, full pulse	Patient returned from critical toward safe state. Regressed. Given further treatment on 2nd day (2)

TABLE I.—*continued*

Case No.	Age and Sex	Agent and Quantity Taken	Duration of Coma before Treatment (Hours)	State before Specific Treatment	Total Specific Treatment (Dose in Grammes)	Dose (in Grammes) Required to Produce "Safe State"	State after Treatment	Comments
24	(*continued*)				NP13 D.A.P.T.	NP13 D.A.P.T.		
				P. 108, R. 16, B.P. 75/50. Areflexia, atonia, fixed pupils. Slight cyanosis and poor peripheral return. No response to supraorbital pressure	(2) 1·35 0·57 in 2½ hours	1·35 0·57 in 2½ hours	P. 108, R. 24, B.P. 90/55, T. 99° F. (37·2° C.). Reflexes present, fair tone, good plantar response. Good peripheral return. No cyanosis. Swallowing. No response to supraorbital pressure. Brisk pupillary light reflex	5 hours later: Some regression; "intradex" substituted for 5% glucose. 10 hours later: Developing R. basal pneumonia; T. 101·5° F. (38·6° C.). Has allergic penicillin rash. Given aureomycin. Regressed. Given further treatment (3)
				P. 128, R. 26, B.P. 80/60. Atonia, areflexia, slight pupillary reflex. No response to supraorbital pressure. Peripheral return adequate	(3) 0·5 0·15 in 45 minutes	0·5 0·15 in 45 minutes	P. 132, R. 28, B.P. 90/60. As in (2) above. Conjunctivae still chemotic. Response to supraorbital pressure	3rd day: Again some regression. Forced cough occasionally present. Oral therapy by Ryle's tube. Right chest consolidated. Regressed again on 4th day. Given further treatment (4)
				P. 92, R. 18, B.P. 60/35. Atonia, areflexia, mildly cyanosed. Poor peripheral return. Right lung consolidated, some dullness left base	(4) 0·95 0·29 in 1½ hours	0·95 0·29 in 1½ hours	P. 96, R. 16, B.P. 110/65. Active reflexes, good tone. Swallowing, moving jaw. Colour peripheral return good. No response to supraorbital pressure	6 hours later: Slight regression, but B.P. 125/70. Regression on 5th day. Given further treatment (5)
				P. 108, R. 18, B.P. 110/65. Sluggish reflexes slight tone; pupillary reflex good. Right chest still consolidated. No response to supraorbital pressure	(5) 0·3 0·1 in 40 minutes	0·3 0·1 in 40 minutes	P. 100, R. 15, B.P. 120/75. Brisk reflexes, good tone. Definite response to supraorbital pressure, swallowing and chewing. Raising eyelids. Colour and peripheral return good	6 hours later (6th day): Some regression, but condition satisfactory; good urinary output. Given further treatment (6)
				P. 100, R. 18, B.P. 115/75. Decreased reflex response, slight tone. No response to supraorbital pressure. Colour and peripheral return good	(6) 0·45 0·14 in 45 minutes	0·45 0·14 in 45 minutes	P. 84, R. 18, B.P. 125/65. Brisk reflexes and good tone; yawning, coughing, swallowing, moving jaw and eyelids. Groaning. Marked response to supraorbital pressure	14 hours later (7th day): Some regression, but condition satisfactory. Given further treatment (7)
				P. 108, R. 25, B.P. 115/65. Decreased tone and reflexes. No response to supraorbital pressure. Colour and peripheral return good. Right lung still fully consolidated	(7) 0·65 0·19 in 55 minutes	0·65 0·19 in 55 minutes	P. 108, R. 22, B.P. 135/75. Brisk reflexes, good tone; swallowing, coughing, moving jaw, and opening eyes. Groaning	Large quantities of barbiturate still present in urine. 15 hours later: Some regression. Given further treatment (8). Patient started menstruating. Serum electrolytes: Sodium 139 mEq/l.; potassium, 3·4 mEq/l.; proteins, 6 g. %; *p*H of serum —7·4. Given 8 g. KCl per day
				P. 84, R. 22, B.P. 120/65. Decreased tone and reflexes. Some response to supraorbital pressure. Colour and peripheral return good	(8) 0·25 0·08 in 30 minutes	0·25 0·08 in 30 minutes	P. 104, R. 20, B.P. 135/75. Brisk reflexes, good tone, coughing more strongly. Opening eyes and rejecting oral airway. Groans on supraorbital pressure	Pneumonia resolving; slow progress over next 2 days. Still much barbiturate in urine. Further treatment next day (9)
				P. 108, R. 16, B.P. 105/60. Decreased tone and reflexes. Groaning on supraorbital pressure	(9) 0·15 0·04 in 15 minutes	0·15 0·04 in 15 minutes	P. 112, R. 16, B.P. 120/65. Brisk reflexes, good tone. Obeying orders and trying to talk in a slurred voice; moving head and biting airway	No regression; patient talking rationally on 12th day. Very weak. Eating. No apparent residual cortical damage. Good insight into domestic problems. Chest almost clear. Slow progress and uneventful recovery
1	F 26	Cyclobarbitone 3·6 g.	2	P. 88, R. 18, B.P. 105/90. Atonia, areflexia, pupils sluggish to light, no reaction to supraorbital pressure	1·75 — in 95 minutes	0·25 0·35 in 20–30 minutes	P. 92, R. 18, B.P. 115/80. Restless, moaning, retching; brisk reflexes	Patient overdosed, required paraldehyde after 8 hours. 2nd day: Still restless and confused. 3rd day: Quieter. 4th day: Normal, no after-effects
26		Voluntary patient given 0·75 g. sodium pentobarbitone under E.E.G. control	½	P. 84, R. 12. Decreased tone, depressed reflexes, some intercostal paralysis. Slight response to supraorbital pressure	1·0 — in 30 minutes	0·3 —	Reflexes exaggerated, groaning, moving whole body and opening eyes. Flushed, vomiting. Did not wake completely	3 hours later: Flushed, irritable, dizzy, confused; rambling speech. Reflexes exaggerated, tossing in bed, slight muscular twitches of fingers, arms, and isolated facial muscles. P. 92, R. 14, B.P. 100/70. Patient presented with picture of cerebral irritation due to NP13 overdosage. Sedated with paraldehyde, "sodium amytal," and "luminal." Took 2 days to return to normal. There were no residual after-effects, but there was amnesia for the event. E.E.G.: The "spikes" indicative of incipient NP13 toxicity were initially hidden by muscle spikes and appeared only later, whereupon NP13 was stopped

TABLE II.—*Summary of Other Cases Treated*

Case No.	Age (Years) and Sex	Agent and Quantity Taken	Duration of Coma before Treatment Started (Hours)	Complications Present	Regression Present	No. of Treatments Given	Total Dose (grammes)	Comments
2	F 38	Quinalbarbitone ? dose	6	Nil	—	1	NP13 D.A.P.T. 1·8 — in 90 minutes	One of our earliest cases. Patient overdosed. At safe state with 0·5 g. Restless 3 days
3	M 54	"Sedormid" ? dose	14	,,	—	1	0·75 — in 45 minutes	Overdosed. Safe state with 0·4 g. Restless 3 days
4	F 21	Phenobarbitone ? dose	13	,,	—	1	0·45 — in 2½ hours	Some regression 6 hours later, but uneventful recovery
5	F 14	Phenobarbitone ? dose (? also small amount of bromide or paraldehyde)	11	,,	—	1	0·6 — in 2 hours	No regression or signs of toxicity. Uneventful recovery
6	F 27	"Carbrital" ? dose	9	,,	—	1	1·7 — in 1½ hours	Awake 1 hour later. Uneventful recovery
7	F 44	Quinalbarbitone 1·6 g.	7	,,	—	1	0·43 0·1 in 2 hours	No signs of toxicity. E.E.G. 3 days later, normal rhythm
8	M 28	Phenobarbitone ? dose	?	,,	—	1	2·0 — in 50 minutes	Completely conscious after 2 days. Uneventful recovery. Some signs of toxicity due to rapid administration
9	F 32	"Carbrital" (pentobarbitone sodium 1 g., carbromal 2·7 g.)	4	,,	—	1	0·3 0·18 in 25 minutes	Well next day. No signs of toxicity
10	F 49	"Carbrital" and phenobarbitone ? dose	80	Bronchopneumonia and peripheral circulatory failure	Yes	2	0·9 0·5	2nd day co-operative; 5 days later approaching normal
12	M 84	?	?	Bronchopneumonia	,,	2	2·1 0·77	Conscious 2nd day, talking 3rd day, normal 5th day
13	F 28	Bromvaletonum 20 g.	12	Nil	—	1	0·7 0·3 in 1½ hours	Uneventful recovery next day
14	M 42	"Carbrital" (pentobarbitone sodium 3 g., carbromal 8 g.). Phenobarbitone ? dose	12	,,	Yes	2	0·4 0·57	Uneventful recovery
15	F 49	Phenobarbitone 5 g.	12	Peripheral circulatory failure	,,	4	1·55 0·63	Patient took 5 days to return to normal. No after-effects
16	F 23	Quinalbarbitone 2·5 g. Amylobarbitone 2·5 g.	?	Nil	—	1	0·8 0·3 in 2 hours	Well next day. Uneventful recovery
19	M 25	"Carbrital" (pentobarbitone sodium 3 g., carbromal 8 g.)	13	,,	—	1	0·4 0·12 in 40 minutes	,, ,, ,, ,, ,,
20	F 46	Butobarbitone 2–4 g.	14	,,	—	1	0·25 0·1 in 30 minutes	,, ,, ,, ,, ,,
21	F 50	Phenobarbitone 6·5 g.	3	,,	Yes	3	0·85 0·45	Patient took 5 days to return to normal. No after-effects
22	F 22	"Carbrital" (pentobarbitone sodium 1 g., carbromal 3 g.)	8	,,	—	1	0·6 0·18 in 1½ hours	Well next day. Uneventful recovery
23	F 28	"Carbrital" (pentobarbitone sodium 2 g., carbromal 5·6 g.)	3	,,	—	1	0·5 0·17 in 1½ hours	,, ,, ,, ,, ,,
25	M 57	Phenobarbitone 3 g.	30	Peripheral circulatory failure. On noradrenaline drip	Yes	4	1·85 0·63	Conscious after 5 days. Slow subsequent uneventful recovery
27	M 50	Given phenobarbitone sodium 1·4 g. in an attempt to control hiccup over 5 days	—	—	—	1	0·13 0·1 in 20 minutes	Patient initially drowsy, quickly recovered. Subsequent regression, return of hiccups
30	M 53	Pentobarbitone sodium 2·5 g.	7	Nil	—	1	0·3 0·1 in 45 minutes	Uneventful quick recovery
31	F 54	"Carbrital" (pentobarbitone sodium 2 g., carbromal 5·5 g.)	10	,,	—	1	0·5 0·15 in 1½ hours	Quick response, uneventful recovery
32	F 64	Phenobarbitone ? dose	6 days	Early pneumonia	—	1	0·2 0·08 in 20 minutes	Patient not very deep; quick response. Took 3–4 days for full recovery
33	F 38	Quinalbarbitone sodium 3 g. Amylobarbitone sodium ? dose	12	Nil	—	1	— 0·18 over 30 minutes	Patient in light coma at start of treatment. Quick response; no regression; uneventful recovery
34	M 36	Pentobarbitone sodium ? dose	14	,,	—	1	0·15 0·05 over 15 minutes	Patient bright when treatment started. Quick response, uneventful recovery
35	M 65	Phenobarbitone 6 g.	Over 24	Early bronchopneumonia and peripheral circulatory failure	Yes	2	0·95 0·3	Very ill. Good response to safe state with 1st treatment. Regressed. Not fully recovered for 5 days
36	M 57	Phenobarbitone 3 g.	30	Peripheral circulatory failure. Put on noradrenaline drip before specific treatment started	,,	4	0·9 0·33	Very ill. Initial response good, but regressed. Not fully recovered for 5 days
37	F 45	"Carbrital" (pentobarbitone sodium 1·5 g., carbromal 3·5 g.)	6	Nil	—	1	0·25 — in 30 minutes	In deep coma on admission. Recovered suddenly; sat up and talked. No regression; uneventful recovery
38	M 33	Pentobarbitone sodium ? dose	About 12	,,	—	1	0·23 0·24 in 35 minutes	Quick response, uneventful recovery
39	F 66	Phenobarbitone ? dose	12–18	,,	Yes	3	3·0 0·69	Patient in deep coma on admission. Regressed. Not fully recovered for 7 days
40	M 56	"Sedormid" ? dose	About 6	,,	—	1	0·65 0·15 in 40 minutes	Suddenly recovered. Confused and restless. Uneventful recovery
41	F 46	Pentobarbitone sodium 5 g.	17	Peripheral circulatory failure	—	1	0·2 0·3 (given ammonium ββ-methylethylglutaric acid 0·7 g. over 3 hours initially)	The ammonium salt afforded some lightening of the coma, but gave rise to symptoms of cerebral irritation. Subsequent NP13 gave rapid, uneventful recovery
29	F 61	"Carbrital" (pentobarbitone sodium 5 g., carbromal 12 g.)	12	Nil	Yes	2	1·0 0·3 Over 3 hours	The only fatality in the series. See text for case report

used only as supportive measures during the initial acute phase of the coma pending the start of treatment.

NP13 has been used to advantage as an aid in the differential diagnosis of cerebrovascular accident and barbiturate intoxication in a patient whose condition was rapidly deteriorating and in whom no localizing signs were present (Case 28).

Control electroencephalograms (E.E.G.s) were taken in three patients (Cases 11, 15, 22) and one volunteer (Case 26). In ten other cases (7, 10, 16–23) recordings were made at the end of treatment. The volunteer was given an overdose of NP13 in an endeavour to effect immediate and complete awakening, and the E.E.G. showed the characteristic spikes of cerebral irritation. The remaining patients all received a mixture of NP13 and D.A.P.T. In the cases under E.E.G. control treatment was stopped either before, or as soon as, there was any suggestion of sharp wave activity. All records taken after termination of therapy showed varying degrees of abnormality indicated by slow or increased low-voltage fast activity. Serial records revealed a gradual disappearance of these abnormalities. Complete clinical recovery was usually apparent for some time before the E.E.G. pattern became normal, especially in patients who had taken long-acting barbiturates.

Routine investigations were carried out in 14 cases (10, 11, 12, 14–23, 25) during the week following recovery. These included tests of renal and liver function, full blood count, naked-eye and microscopical examination of cerebrospinal fluid, electrocardiography, and estimation of serum electrolyte balance. The only abnormality detected in seven cases (11, 15–17, 20–22) was a low serum potassium value of the order of 3.5 mEq per litre. This was occasionally accompanied by a concomitant imbalance of the other ions.

Case 24 deserves special mention. This patient (probably the most seriously ill patient in our series) was comatose for ten days, and during this period was given nine consecutive treatments with NP13 and D.A.P.T., with eventual restoration to full consciousness. Her subsequent rehabilitation was slow and uneventful. We followed this procedure as we felt that the patient's severe and prolonged coma was in part due to a secondary cerebral hypoxia of hypotensive origin superimposed on the primary barbiturate hypoxia. We were therefore disinclined to give more than minimally adequate doses of NP13 and D.A.P.T. (to maintain the "safe state"), to avoid the risk of excessively stimulating an already overburdened nervous apparatus and mechanism. An adequate blood pressure and high renal output were maintained throughout. Large quantities of barbiturate were still being excreted in the urine seven or eight days after the coma began.

One patient (Case 29) died, but death was not thought to be due to the specific treatment. Details of this case follow.

Report of a Fatal Case

A woman aged 61 took 50 "carbrital" capsules (containing 5 g. pentobarbitone sodium and 12 g. carbromal) about 12 hours before treatment was instituted. On admission: pulse rate 72 per minute; shallow, irregular respirations (rate 32 per minute); blood pressure 120/70 mm. Hg. No reflexes could be elicited. She was atonic, hypothermic (temperature 95° F.—35° C.), and unresponsive to painful stimuli, with unreactive pupils and a poor peripheral return. She was given 1 g. NP13 and 0.3 g. D.A.P.T. in two treatments over three hours. There was a rapid return of reflexes and some response to painful stimuli, but facial twitches suddenly developed and there were signs of respiratory depression. The twitching was quickly controlled with thiopentone sodium; the patient was intubated and artificial respiration started. Owing to a fault in the circuit the patient rebreathed air with a high CO_2 content for several hours before it was discovered. When, eight hours later, in an attempt to promote normal respiration, a small dose of D.A.P.T. (60 mg.) was given in divided doses over 12 minutes, the patient had a unilateral left-sided epileptiform convulsion which 0.4 g. thiopentone sodium failed to control. Lumbar puncture gave a blood-stained cerebrospinal fluid with a protein content of 1,600 mg. per 100 ml. and showing xanthochromia on sedimentation of the red cells. There were no localizing signs of a cerebro-vascular episode.

In spite of prolonged artificial respiration following tracheotomy and the administration of a continuous noradrenaline drip, the blood pressure progressively fell and the patient died.

Significant Post-mortem Findings.—The skull was normal. The arteries to the brain were well preserved and showed minimal atheroma. In the middle cranial fossa there was a little brownish-yellow staining of the dura. Over the parietal surface of the left cerebral hemisphere there was a very small localized area of subarachnoid bleeding, not sufficiently marked to lift the membrane off the brain; there was also a very small amount of subdural bleeding in this area. The brain did not show evidence of compression; it was symmetrical and the convolutions appeared normal. On routine serial section of the substance of the brain no naked-eye abnormality was detected. There was no bruising or evidence of injury on the scalp. The coronary vessels showed marked thickening and calcification. The heart was a little enlarged. No infarction or scarring was visible in the heart wall. There was patchy atheroma of the aorta. Both lungs showed extensive consolidation and waterlogging. The liver and kidney contained ¼ gr. of carbromal and 1/10 gr. of pentobarbitone per lb. (124 and 14 mg. per kg.).

Discussion

There are at present two schools of thought as to the treatment of acute barbiturate intoxication. Both agree that the basis of good management is thorough and intelligent medical care. They are, however, at variance regarding the concomitant use of central analeptics, of which only picrotoxin, leptazol, "geastimol," and occasionally amphetamine and nikethamide are in present-day use.

The conservative school is led by Nilsson, who regards acute barbiturate intoxication as "an anaesthesia which is drawn out to last for days instead of lasting, like a common so-called surgical anaesthesia, for at most a few hours," and who therefore treats the condition "in accordance with anaesthesiological principles." Nilsson (mortality rate 2–3%), Locket and Angus (mortality rate 3–4%), and Clemmesen (mortality rate 1.6%) relied solely on a carefully planned medical regimen. None used central analeptics, and indeed all stressed the dangers involved in their use. Their excellent results afford strong support for their expectant routine of treatment.

This mode of management has been criticized by the protagonists of the analeptic school of treatment led by Koppanyi and Fazekas (1952), who insist that there is still a definite place for central analeptics, especially in cases of severe barbiturate intoxication.

In the absence of adequate information concerning the mode of action of central analeptics (Eckenhoff *et al.*, 1949), and in the presence of many animal experiments (Maloney, 1935, 1936; Mousel and Essex, 1941; Schmidt, 1945; Davis *et al.*, 1944) and clinical data (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954) indicating the dangers involved in their use, we find ourselves drawn more closely to the conservative school of treatment led by Nilsson. There appear to be, however, two disadvantages to this conservative management. (1) One can never be sure, with a patient in deep barbiturate coma, if and when he will regain consciousness, and if and when complications which could alter the whole outlook of the case will develop. Naturally, the more prolonged the coma the greater would be the risk of this occurring, despite the most scrupulous medical care. (2) The management of a case of prolonged barbiturate coma presents a serious problem in a busy overcrowded hospital. Our new method of treatment helps by bringing such a patient in two hours to a desired state of light anaesthesia—the "safe state"—from which

spontaneous recovery to full consciousness usually occurs within eight hours. It thus removes the immediate risk to the patient's life, prevents the onset of complications often associated with prolonged barbiturate coma, and also promotes a speedier discharge from hospital. We do not attempt to restore full consciousness, for not only have we found this to be impossible in many cases, but there is also the risk, especially when using NP13 alone, of producing an excited, irritable patient who often needs prolonged sedation. Our inability to awaken the patient fully may be due to a concomitant cerebral hypoxia and disordered cerebral metabolism resulting from the prolonged action of the barbiturate (Bailey *et al.*, 1953; Bain, 1952; Brody and Bain, 1954), and naturally time must be allowed for restitution to normal.

We have previously suggested that NP13 in therapeutic doses may exert a direct antagonism to the barbiturate, as indicated by the fact that rabbits can be put to sleep or awakened almost at will by the alternate intravenous administration of thiopentone sodium and NP13. This change can be rapidly and repeatedly effected without any apparent harm to the animal. The antagonism is further supported by our observations, both in patients suffering from deep barbiturate coma and in dogs under deep pentobarbitone anaesthesia, of a rapid clinical and somewhat slower encephalographic recovery to the unnarcotized state after the administration of NP13 or a mixture of NP13 and D.A.P.T. This is in direct contrast to the findings of most workers, who agree, on both clinical and experimental grounds, that all of the central analeptics in current use, except possibly picrotoxin, are of little value in the treatment of deep barbiturate coma. It is also in direct contrast to the observations of Mousel and Essex (1941), who found that nikethamide, leptazol, picrotoxin, α-lobeline, and geastimol all failed to produce demonstrable change in the E.E.G. of dogs deeply anaesthetized with amytal.

Present evidence suggests that NP13 is the best substance yet used in the treatment of barbiturate coma, and in combination with D.A.P.T. should ensure a quick, safe recovery without risk of convulsions and secondary depression, which often follow treatment with central analeptics.

Finally we wish to emphasize the value of D.A.P.T. not only as a barbiturate antagonist, but also as a potent, non-specific respiratory stimulant. This latter property has been specially important in the management of barbiturate coma where pneumonic complications have supervened. We elsewhere (Shulman and Shaw, 1955) suggest other clinical uses for D.A.P.T., especially in relieving prolonged and severe pain and in the fields of anaesthesia and obstetrics.

Summary

A new method of treating acute barbiturate intoxication, incorporating the use of two new substances—$\beta\beta$-methylethylglutarimide (NP13) and 2:4-diamino-5-phenylthiazole hydrobromide or hydrochloride (D.A.P.T.)—has been outlined. It compares more than favourably with other methods in that it minimizes the risk of complications and removes the need for strict and prolonged medical and nursing care without incurring the risk of convulsions and secondary depression sometimes accompanying treatment with analeptics.

Animal and clinical investigations have revealed that NP13 and D.A.P.T. possess a high therapeutic index and quickly relieve the acute phase of severe barbiturate coma, whereby the patient is deliberately restored to an easily manageable state of light anaesthesia—the "safe state," from which spontaneous recovery to full consciousness usually occurs within eight hours.

The pharmacology of NP13 and D.A.P.T. has been briefly described, and evidence presented to suggest that NP13, which has a structural resemblance to the barbiturate ring system, may exert its effect by a direct antagonism to the offending barbiturate.

Results of treatment with these drugs in 41 cases of barbiturate intoxication have been summarized.

It is suggested that these substances may provide an effective means of controlling anaesthesia induced by barbiturates, both in enabling a rapid recovery to the conscious state where desired and in counteracting any emergency such as laryngeal spasm.

The value of D.A.P.T. as a non-specific respiratory stimulant is pointed out and suggestions are made as to its further clinical use.

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The role of the family doctor in research was discussed by Professor J. M. MACKINTOSH in the first John Matheson Shaw lecture, delivered at the Royal College of Physicians of Edinburgh last November. Tracing the history of the general practitioner through the nineteenth cenury, Professor Mackintosh showed that it was not until the end of that period that research by general practitioners came to be taken seriously. To-day the College of General Practitioners can guide his investigations, making his contribution part of a large survey, and the Public Health Laboratory Services provide him with facilities he used to lack. In several fields the family doctor has an advantage over the specialist; with his knowledge of family background perhaps extending over two or three generations, he can report on hereditary defects; again, the knowledge of background and environment is vital to a study of mental illness and stress diseases. The effectiveness of new drugs and vaccines, the epidemiology of common ailments, the incubation periods of well-known infections can all be studied best in general practice, and "we all know that the family doctor is the only medical worker to-day to see disease in its early stages." Professor Mackintosh suggested that the chief obstacle to general-practitioner research lay in the defective undergraduate training, which did not, for instance, include even elementary statistics, and the chief incentive is the co-operation between doctors and the College of General Practitioners.

MEGALOBLASTIC ANAEMIA OF PREGNANCY AND THE PUERPERIUM

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Investigation of patients with megaloblastic anaemia of pregnancy and the puerperium is handicapped by the urgency with which treatment must be carried out and by the tendency of the anaemia to remit spontaneously after delivery. Strauss and Castle (1933) suggested that this anaemia was due to a temporary reduction in the secretion of intrinsic factor, but the failure of parenteral liver extracts and vitamin B_{12} to bring about remission in most cases has made it clear that this cannot be the only explanation. Three cases have been described in which defective absorption of fat was discovered on subsequent admission to hospital (Davidson, 1948; Tuck and Whittaker, 1950; Thompson and Ungley, 1951), and Tuck and Whittaker (1950) have proposed that, in some instances at least, the underlying mechanism may be an occult idiopathic steatorrhoea, which is unmasked by pregnancy. In the present observations on nine patients, particular attention has been directed to the detection of abnormalities of gastric secretion and defects of the absorption of fat and labelled vitamin B_{12} from the intestine. We show that there was no evidence of reduction in the secretion of intrinsic factor or in the absorption of fat in these patients.

Clinical Features

The salient clinical features are presented in Table I. Four women were investigated before term and the remaining five were seen after delivery; in all cases the diagnosis was confirmed by finding megaloblastic changes in the sternal marrow. Of particular interest is the high incidence of complications such as vomiting, diarrhoea, and haemorrhage, which might tend to decrease the supply of or increase the demand for haemopoietic factors during pregnancy and the puerperium. The tongue was sore in three patients. There was atrophy of the papillae in four patients—complete in two and confined to the edge of the tongue in two. Aphthous ulcers were present in four patients, three of whom had leucopenia. The spleen was palpable in two patients, in whom the level of haemoglobin was less than 5 g. No neurological abnormality was detected in any of the patients.

Treatment was with folic acid by mouth or vitamin B_{12} by injection. Folic acid was given in a dose of 20 mg. daily. Vitamin B_{12} was given on a single day only, in a dosage of 2,000 μg.; this was the "flushing dose" which was employed in measuring the excretion of labelled vitamin B_{12} in the urine. In Case 8 only 100 μg. of vitamin B_{12} was given.

Of the three patients seen three weeks or more before delivery, one responded well to folic acid alone, another failed to respond to vitamin B_{12} but subsequently improved with folic acid, and the third showed no improvement up to the time of delivery with combined folic acid and vitamin B_{12} therapy. A fourth patient was treated with vitamin B_{12} and folic acid one week before delivery without apparent effect, but gradual improvement occurred during the puerperium.

In three patients the diagnosis was made early in the puerperium. An optimal response followed treatment with vitamin B_{12} in one and folic acid in another. The third received both vitamin B_{12} and folic acid, and showed a progressive increase in haemoglobin, although the reticulocytes did not rise above 3%. Since spontaneous remission is common following delivery, it is not certain that these responses were due to specific therapy.

Two patients were seen with severe anaemia six weeks after delivery. There was no response to vitamin B_{12} over a period of eight days in Case 8, but prompt symptomatic and haematological remission followed the administration of folic acid. Case 9 was transfused initially and then treated with vitamin B_{12} with an optimal reticulocytosis and rise in haemoglobin and the haematocrit reading.

Special Investigations

(A) Methods

1. *Gastric Secretion.*—Gastric acidity was measured directly in seven subjects and indirectly by the "diagnex" technique (Conway and Meikle, 1953) in one (Case 5). In two patients free acid was found in the resting juice and no stimulant was given. Fractional test-meal examinations were carried out on four patients with histamine and one patient with gruel. The urinary excretion of uropepsinogen over a 24-hour period was measured in seven subjects (Aitken *et al.*, 1951).

2. *Gastric Biopsy.*—Biopsy of the gastric mucous membrane was carried out in four patients, using Wood's flexible gastric biopsy tube (Wood *et al.*, 1949).

3. *Absorption of Vitamin B_{12}.*—The absorption of vitamin B_{12} was tested by measuring the amount of radioactivity which was found in the faeces after an oral dose of 0.5 μg. of vitamin B_{12} labelled with cobalt[60] (Heinle *et al.*, 1952). This gave an indirect assessment of the secretion of

TABLE I

Case	Age	Previous Pregnancies	Diagnosis of Anaemia	Complicating Features	Hb Before Therapy (g./100 ml.)	Response to Therapy
1	22	4	Ante partum 4 weeks	Fifth pregnancy within 5 years	4·6	Transfused—Hb 6·8 g. Folic acid—good response
2	18	0	Ante partum 4 weeks	Twin pregnancy	9·8	B_{12}—no response 14 days. Folic acid—good response
3	20	0	Ante partum 3 weeks	Vomiting and anorexia throughout pregnancy	9·9	B_{12} and folic acid—no improvement up to time of delivery
4	23	1	Ante partum 1 week	Poor diet; hypertension	10·3	B_{12} and folic acid—no reticulocytosis, improved post partum
5	34	2	Post partum 1 week	Very poor diet; appendicectomy in first trimester	8·9	B_{12}—good response
6	28	2	Post partum 2 weeks	Anorexia, diarrhoea, mild toxaemia, and post-partum haemorrhage	3·9	Transfused—Hb 9·7 g. Folic acid—good response
7	20	2	Post partum 1 week	Post-partum haemorrhage; third pregnancy in 3 years	9·2	B_{12} and folic acid—moderate rise Hb, reticulocytosis 3%
8	22	0	Post partum 6 weeks	Post-partum vomiting; puerperal fever—? endometritis	5·3	B_{12}—no response 8 days. Folic acid—good response
9	29	1	Post partum 6 weeks	Ante-partum diarrhoea; breast abscess first week post partum	4·7	Transfused—Hb 9·6 g. B_{12}—good response

intrinsic factor. In six patients a parenteral injection of 2,000 μg. of non-radioactive vitamin B_{12} was given with the oral dose in order to rid the body of as much of the absorbed radioactivity as possible (Schilling, 1953). Normally 15% or more of the oral dose of 0.5 μg. of Co^{60}-vitamin B_{12} is excreted in the urine with this technique (Callender and Evans, 1955). The collection of stools was incomplete in Case 3, and only the radioactivity in the urine was measured.

4. *Absorption of Fat.*—The absorption of fat was estimated in six of the subjects by a four-day fat balance with a measured dietary intake of 70 to 100 g. of fat daily.

5. *Serum Vitamin B_{12}.*—The level of vitamin B_{12} in the serum was determined by microbiological assay, in two cases with *Euglena gracilis* and in four cases with *Lactobacillus leichmannii.*

TABLE II

Patient	Free Acid in Gastric Juice	Uropepsinogen Excretion (Units/24 hr.)	Percentage of Oral Dose of Co^{60}-vitamin B_{12} in Faeces	Fat Absorption (% of Dietary Intake)	Serum Vitamin B_{12} (μμg./ml.)
Normal values ..		50+	9–47	90+	100+
1	0	140	30 ; 17	—	—
2*	+	9	18	91	430
3	Not tested	—	(23)†	—	—
4	+	116	28	95	140 ; 110
5*	+	310	16	96	310
6*	0	161	42 ; 33	—	—
7	+	132	28	96	260
8*	+	164	36	95	190 ; 175
9	+	48	28	96	220

* Gastric biopsy. † Radioactivity in urine.

(B) Results (Table II)

1. *Gastric Secretion.*—The fractional test meal revealed achlorhydria in two patients, but in one of these (Case 1) the uropepsinogen excretion was within normal limits, and in the other (Case 6) the biopsy showed no atrophy of the gastric body glands. Uropepsinogen excretion was low in two patients, within the range encountered in pernicious anaemia, but in both of them free acid was present in the gastric juice.

2. *Gastric Biopsy.*—Histological examination of the gastric mucosa revealed no abnormality. There was evidence of superficial gastritis in Case 6, but no atrophy of the gastric body glands was noted.

3. *Absorption of Vitamin B_{12}.*—The absorption of vitamin B_{12} was normal in all nine patients, implying that the secretion of intrinsic factor was adequate.

4. *Absorption of Fat.*—The absorption of fat was within normal limits in the six patients tested. The low normal result on the basis of a four-day fat balance does not absolutely exclude the possibility of steatorrhoea in Case 2.

5. *Serum Vitamin B_{12}.*—Normal quantities of vitamin B_{12} were present in the serum of five patients. The values in Case 4 are just above the range observed in untreated pernicious anaemia, and might be explained by the grossly inadequate diet which she took throughout her two pregnancies and the intervening period.

Discussion

The preceding investigations do not provide conclusive evidence of the nature of the disturbance of haemopoiesis in megaloblastic anaemia of pregnancy and the puerperium or of its pathogenesis. The secretion of intrinsic factor, as determined by the absorption of radioactive vitamin B_{12}, was normal and there is therefore no support for the theories of Strauss and Castle (1933). The absorption of fat was also normal in our patients, as it was in six cases of megaloblastic anaemia of pregnancy recently studied by Moore *et al.* (1955). It must therefore be concluded that, though megaloblastic anaemia in pregnancy may occasionally be due to adult coeliac disease, this is by no means a common cause.

Although the absorption of vitamin B_{12} is normal the possibility exists of a deficiency of the vitamin in the diet. This is probably not uncommon in India (Das Gupta, 1954), and it has been described in Europe. Nieweg *et al.* (1954) report two patients responding to vitamin B_{12} therapy in whom the evidence favours a deficiency of the vitamin. In one the serum vitamin B_{12} was very low (40 μμg. per ml.), and in the other the blood folic acid was normal. In 20% of a group of patients studied during pregnancy and lactation, Heinrich (1954) found low serum vitamin B_{12} levels and reduced excretion of vitamin B_{12} in the urine, although there was no evidence of macrocytic anaemia. Oral administration of vitamin B_{12} was effective in restoring normal serum levels and urinary excretion in these patients, and Heinrich suggested the existence of a state of hypovitaminosis-B_{12} due to increased demands for the vitamin during pregnancy and lactation.

However, Mollin and Ross (1954) report serum vitamin B_{12} levels in 31 cases of megaloblastic anaemia of pregnancy and the puerperium, and in only two were the levels as low as is seen in untreated cases of pernicious anaemia. In our cases, likewise, the level of vitamin B_{12} in the serum was within normal limits. Hence it would appear that, although vitamin-B_{12} deficiency may occur in Europe, it is not commonly responsible for the development of megaloblastic anaemia in pregnancy. In the two women who improved with vitamin B_{12} therapy in the present series the response may have been mediated by some indirect mechanism, related to the massive size of the dose, for in both of them the serum levels of vitamin B_{12} were normal. This conclusion is supported by the work of Moore *et al.* (1955), who obtained a satisfactory response to vitamin B_{12} in 13 out of 17 cases of megaloblastic anaemia of pregnancy by giving massive doses, of the order of 1,000 μg. Five of their patients were treated before delivery and 12 after. The four women who did not respond to vitamin B_{12}, which in two instances was pushed to 5,000 μg., responded to folic acid.

At present it is difficult to assess the folic acid status of the organism other than by the response to treatment. Folic acid in large doses is usually effective in the megaloblastic anaemia of pregnancy, both before and after delivery. This observation favours a folic acid deficiency, though this deficiency, like that of vitamin B_{12}, is more likely to be relative than absolute, for remission may occur after delivery in patients who receive no treatment at all.

It seems likely that patients with megaloblastic anaemia of pregnancy and the puerperium do not represent a homogeneous group, and this may explain the variable findings and response to therapy. Complications of pregnancy and the puerperium occur frequently in relation to megaloblastic anaemia. Toxaemia and infection may interfere with the utilization of haemopoietic factors; haemorrhage and multiple or rapidly repeated pregnancies may increase the demands; while poor diet and gastro-intestinal upsets reduce the natural supply. However, in some patients pregnancy alone may induce the anaemia, and in such cases the cause appears to be the development of resistance to vitamin B_{12} and folic acid.

Summary

Nine patients with megaloblastic anaemia of pregnancy and the puerperium have been studied. The incidence of complications of pregnancy and the puerperium was high.

No abnormality in the secretion of intrinsic factor or the absorption of fat was discovered in any case.

The serum vitamin B_{12} levels were normal.

In women treated before delivery folic acid was more effective than vitamin B_{12}.

Although an absolute deficiency of folic acid cannot be excluded, the anaemia seems more likely to be due to resistance to the action of the haemopoietic factors than to deficiency.

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MEGALOBLASTIC ANAEMIA FOLLOWING ANTICONVULSANTS

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Two cases of megaloblastic anaemia occurring in epileptics who had been taking phenobarbitone and phenytoin were reported by Badenoch (1954), who suggested that the anticonvulsants might have played a part in the production of the anaemia. Other cases have been reported by Hawkins and Meynell (1954), Chalmers and Boheimer (1954), and Rhind and Varadi (1954).

In April, 1954, we first encountered a megaloblastic anaemia in a patient who had been receiving phenytoin and phenobarbitone. In the absence of any obvious cause we speculated whether anticonvulsant drugs could have had any causative relationship. Our suspicions were strengthened when in July a further epileptic patient under our care developed a megaloblastic anaemia which had no obvious cause. The cases reported recently, together with the cases we now record, seem to indicate that megaloblastic anaemia may arise after the prolonged use of anticonvulsant drugs, and that this anaemia is probably due to phenytoin.

Case 1

A man aged 28 was admitted to Prestwich Hospital with an epileptic psychosis in August, 1952. He had suffered from major and minor fits for seven years and had been taking both phenytoin and phenobarbitone for at least eighteen months. At the time his anaemia was detected he was taking phenytoin 1½ gr. (100 mg.), and phenobarbitone, ¼ gr. (50 mg.), thrice daily. He was a good eater and was on a full mixed diet. There was no history of steatorrhoea.

On April 23, 1954, he was noted to be pale and he complained of weakness. Physical examination revealed nothing beyond pallor of skin and mucous membranes and a loud apical systolic murmur. A blood count showed: haemoglobin, 50%; red cells, 2,660,000 per c.mm.; white cells, 6,800 per c.mm. (polymorphs 48%, lymphocytes 50%, monocytes 2%). Anisocytosis and poikilocytosis were present. A fractional test meal revealed a small quantity of free acid. Sternal marrow puncture revealed megaloblastic erythropoiesis, the predominant cells being early and intermediate megaloblasts. The white-cell series showed early forms, some of which were larger than normal.

On May 4 vitamin B_{12} was started (100 μg. daily), but in spite of this his blood picture continued to deteriorate and there was no reticulocyte response. By May 10 the blood count was: haemoglobin, 25%; red cells, 1,800,000 per c.mm.; white cells, 3,200 per c.mm.; and reticulocytes, 3%. His physical condition was unaltered. He had a smooth tongue but no active glossitis, a loud apical systolic murmur, and high pulse pressure (B.P. 110/50). There was no evidence of subacute combined degeneration of the cord or any clinical evidence of steatorrhoea or liver disease.

On May 10 he was put on oral folic acid, 5 mg. four times a day. On the 11th his reticulocytes were 5%, and by the 13th they had reached 8%. In addition to folic acid, 20 mg. daily, he received a crude liver preparation ("hepatex T," 4 ml. daily) from May 11 to 13. Otherwise he was maintained solely on folic acid.

On the 13th he was transferred to the Manchester Royal Infirmary under the care of Dr. J. F. Wilkinson. His reticulocytes reached a peak of over 30%, and on his return to Prestwich Hospital on June 2 his haemoglobin had reached 70%. By July 9 the blood count showed: haemoglobin, 90%; red cells, 5,000,000 per c.mm.; white cells, 13,600 (normal differential).

He was discharged home in August, his mental state having improved. He remained on phenytoin and phenobarbitone throughout his illness, and at the time of discharge was taking folic acid, 20 mg. daily.

Case 2

A 26-year-old male epileptic had suffered from epilepsy following a head injury at the age of 5 which had left him with a left hemiparesis. He was also suffering from an epileptic psychosis. He had been on phenobarbitone and phenytoin since 1950. In May, 1954, he was put on to primidone, 0.25 g. thrice daily, in addition to phenytoin, 1½ gr. (100 mg.), and phenobarbitone, ¼ gr. (32 mg.), thrice daily to obtain better control of his fits. He was a good eater and was on a full mixed diet. There was no history of steatorrhoea.

Physical examination on August 24, 1954, revealed intense pallor, a left hemiparesis, an apical systolic murmur, and a blood pressure of 140/70 mm. Hg. He had mild hypertrophy of the gums but no significant glossitis. There was no evidence of subacute combined degeneration of the cord or any clinical evidence of steatorrhoea or liver disease. A blood count showed: haemoglobin, 28%; red cells, 1,620,000 per c.mm., white cells, 3,600 per c.mm. (polymorphs 31%, lymphocytes 64%, monocytes 3%, eosinophils 3%). Anisocytosis, poikilocytosis, punctate basophilia, Howell–Jolly bodies, and Cabot rings were obvious in the blood film. Sternal marrow puncture showed a megaloblastic marrow, early and intermediate megaloblasts predominating. No abnormality was noted in the white-cell series.

A fractional test meal with histamine showed free acid present. There were no fat globules in the faeces, and faecal-fat estimation showed total fat 28%, with a normal split/unsplit ratio. The glucose-tolerance test showed normal

absorption of glucose (fasting blood sugar, 85 mg. per 100 ml.; 30 minutes, 150 mg.; 60 minutes, 170 mg.; 90 minutes, 140 mg.; 120 minutes, 80 mg.). Liver-function tests were normal (serum bilirubin, 0.4 mg. per 100 ml.; serum alkaline phosphatase, 7.5 King–Armstrong units; thymol turbidity, 2 units; thymol flocculation, 0; colloidal gold, 0).

On August 25 he was started on vitamin B_{12} (100 μg. intramuscularly daily). By the 28th he had still shown no reticulocyte response (reticulocytes remaining stationary at 1%). As the blood picture was deteriorating (haemoglobin, 24%; red cells, 1,300,000 per c.mm. on the 28th) and he was having occasional major fits, he was started on folic acid, 10 mg. twice daily.

On August 30 the reticulocytes were 3%, but on the 31st they rose to 12%. By September 2 a reticulocyte response of 30% had been achieved. The blood picture improved rapidly until on October 12 it showed: haemoglobin, 90%; red cells, 4,980,000 per c.mm.; white cells, 7,800 per c.mm. (normal differential count). The patient is now in good general health and is being maintained on folic acid, 20 mg. daily. He has continued on phenytoin and phenobarbitone throughout, primidone having been discontinued when his anaemia was first noted.

Discussion

Megaloblastic erythropoiesis is found in pernicious anaemia, the sprue syndrome, abnormalities of the gastro-intestinal tract, nutritional deficiency, diphyllobothrium infestation, and, rarely, in liver disease. Recently, megaloblastic anaemia has been reported in patients who had been receiving anticonvulsants (Badenoch, 1954; Hawkins and Meynell, 1954; Chalmers and Boheimer, 1954; Rhind and Varadi, 1954).

Our two cases were encountered among the epileptic patients in a large mental hospital. The type of patient restricted full investigation, but in both cases the well-known causes of megaloblastic anaemia did not seem to be present. Free acid was found in the gastric juice, there was no evidence of nutritional deficiency or of steatorrhoea or liver disease, and there was nothing to suggest organic disease or previous surgical intervention in the gastro-intestinal tract. Both cases responded well to folic acid, but the clinical impression was that vitamin B_{12} was ineffective.

In Case 1 no reticulocyte response was obtained after six days' treatment with vitamin B_{12}. In Case 2 there was no reticulocyte response five days after commencing vitamin B_{12}, although a response appeared on the sixth day (three days after the start of folic acid treatment). In both cases a good reticulocytosis followed the use of folic acid, and with this drug alone the blood picture was restored to normal and maintained at this level. Both cases had been on phenytoin and phenobarbitone for a period of years, and both continued to receive these drugs during their illness.

Vitamin B_{12} resistance has been reported in all the other cases except one of those reported by Badenoch (1954). Folic acid produced a favourable response in the other recorded cases.

The mechanism of this type of anaemia is obscure. There are numerous instances of the effects of the hydantoins, particularly methoin, upon bone marrow, but only agranulocytosis and aplastic anaemia have been reported in the past (Jones, 1951; MacArthur, 1952). Phenobarbitone rarely causes marrow damage, although a few cases of agranulocytosis have been recorded (Watkins, 1933). Primidone was given to one of our cases, and Chalmers and Boheimer had one of their patients on the drug. Serious blood dyscrasias, however, do not seem to have been recorded in trials so far with this drug, though the fact that it is a dione and a relatively new addition to therapeutics suggests that we may see such results in the future.

Phenytoin would appear to be responsible for the megaloblastic anaemia in these cases. It was the only drug used in the case recorded by Hawkins and Meynell, and it had been used in all other cases reported, although, in these, other drugs had been given in conjunction with phenytoin. If phenytoin is responsible it is remarkable that no previous cases of this type of anaemia associated with the drug have been recorded, for it has been in use since 1938. There is the possibility that previous cases have been dismissed as idiopathic megaloblastic anaemias and the relationship to phenytoin has not been recognized. Another possibility has been suggested by Hawkins and Meynell, to the effect that anaemia may appear only if the patient has taken the drug for a long time. Their patient had been on phenytoin for 13 years. However, most of the recorded cases were on phenytoin for much shorter periods, although the length of time on the drug has been more in the nature of years than months. A further interesting point is that, whilst the number of epileptics on phenytoin is enormous, this complication appears to be a rarity. At this hospital 75 other epileptics receiving anticonvulsant drugs have been screened so far, but none has shown any evidence of anaemia, though in age, type of epilepsy, food, and living conditions, in addition to anticonvulsant medication, they closely resemble the two recorded cases.

Hawkins and Meynell suggest that phenytoin may either affect absorption of haematopoietic factors or act as a folic acid antagonist. In only one case, that of Rhind and Varadi, has there been evidence of malabsorption, and even this was inconclusive. The normal vitamin B_{12} serum levels in those cases in which this has been determined (Badenoch, 1954; Chalmers and Boheimer, 1954; Rhind and Varadi, 1954), and the excellent response to folic acid, suggest that this anaemia is essentially a folic acid deficiency, whatever its precise mechanism. It is extremely difficult to produce a folic acid deficiency in the experimental animal, but, in man, megaloblasts have occasionally been found in the bone marrow in cases of acute leukaemia treated by aminopterin (Stickney, 1952). Wintrobe (1951) reports that in pigs a vitamin B_{12} refractory megaloblastic anaemia can be produced, but only by reducing dietary vitamin B_{12}, excluding folic acid from the diet, and giving a folic acid antagonist in conjunction with succinylsulphathiazole. This porcine anaemia responds promptly to folic acid and resembles the anaemia in the cases on phenytoin reported here.

Whatever the mechanism, it seems essential that epileptics treated with anticonvulsants be watched for the possible advent of this anaemia. The severity of the condition and the excellent response to folic acid make this imperative. Further work will be necessary to elucidate the precise mechanism involved and to produce means of preventing this complication.

Summary

Two cases of megaloblastic anaemia which developed after the prolonged use of anticonvulsants are recorded. Both cases responded well to folic acid, and the evidence suggested that they were refractory to vitamin B_{12}. The literature is briefly reviewed and possible causative mechanisms of this anaemia are discussed.

Thanks are due to Dr. J. P. McGuinness, medical superintendent of Prestwich Hospital, for permission to record these two cases; to Dr. J. F. Wilkinson and Dr. M. C. G. Israëls for help with the treatment of Case 1; and to Mr. T. Read for the laboratory procedures.

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LIPODYSTROPHIA PROGRESSIVA AND TEMPORARY HYDRONEPHROSIS

BY

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If the association of two diseases in a patient is not fortuitous their relationship to each other may throw light on the aetiology of one or both diseases. Lawrence's (1946) study of a woman with lipodystrophia progressiva and insulin-resistant diabetes supports the concept of two types of diabetes mellitus and suggests the simple explanation that the elderly obese person develops diabetes because she is unable to convert any more carbohydrate into fat.

In this paper the association of temporary hydronephrosis with lipodystrophia progressiva is reported and the renal disorders which have been described with this disease are reviewed. It is suggested that in some of the case reports the renal changes may have been similar to those present in the patient described here.

Gross hydronephrosis can develop in a week and disappear completely if the obstruction is removed early enough, and the term "temporary hydronephrosis" has been used to describe these transient changes (Fowler and Frankel, 1947).

Ellis (1951), writing about lipodystrophia progressiva, mentions the association of this condition with renal disease. He makes a brief reference to the occurrence of oliguria in Gerhartz's case (1916). The daily urinary output of this patient was 400–1,100 ml., and it is difficult to believe that this is a significant oliguria. Klien (1921) reports on a patient with lipodystrophy and mentions polyuria. Recently a patient with this disease was shown at the Royal Society of Medicine (Tizard, 1954), and the summary of the case included the information that "she is said to drink and void excessive quantities of fluid." The glucose-tolerance test in this patient was normal, but full urinary investigations including a pyelogram had not been done. Following the paper by Lawrence (1946) on the association of lipodystrophy and diabetes, any patient with lipodystrophy complaining of thirst and polyuria may be examined for further evidence of diabetes mellitus only, as happened to our patient, when studied for a short period at another hospital.

In 1932 two cases were reported in which lipodystrophia progressiva and uraemia occurred in the same patient. They were both thought to have had chronic nephritis, but in neither did the diagnosis appear likely, nor was it confirmed. They both had unusual clinical features in common with the patient described in the present paper.

Horton and Emmett (1932) report the case of a woman of 61 with a history of increasing nausea for one year with occasional attacks of vomiting. The patient was alert, and physical examination was essentially negative except for lipodystrophy affecting the legs. There were no symptoms or signs suggesting uraemia. On admission the blood urea was 400 mg. per 100 ml. After five weeks on a diet containing 25 g. of protein and 3–4 litres of fluid daily, the blood urea fell to 60 mg. per 100 ml. It was stated that pus cells, grade III, were present in the urine, but no mention of urine culture was made. The renal lesion was diagnosed as chronic diffuse glomerulonephritis after the possibility of polycystic kidneys had been considered and dismissed, as no enlargement of the kidneys could be found on abdominal palpation.

Berger (1932) reported the case of a woman aged 26 who developed lipodystrophy at the age of 3½ years. Pyelitis occurred at 6 and another attack a year later. At the age of 19 the blood pressure was found to be raised and albumin was present in the urine. A diagnosis of acute exacerbation of chronic nephritis was made. Following a severe reaction to vaccination, the patient for a short time passed into uraemic coma. During the next seven years she remained well, and clinical examination at the end of this period was essentially negative except for the lipodystrophy. The blood urea was then 21 mg. per 100 ml.

Igersheimer (1948) described the case of a patient who had lipodystrophia progressiva, bilateral hydronephrosis with aberrant renal arteries, and other congenital abnormalities.

Case Report

The patient was the youngest of four children. Her parents and siblings were healthy. At the age of 2½ years she had scarlet fever and was in bed for three months with subsequent "kidney trouble." She had several attacks of sore throat until tonsillectomy at the age of 5. Between the ages of 5 and 9 she remained well except for mild attacks of measles, chicken-pox, and rubella. In 1950, at the age of 9, she was referred to the out-patient department with a ten-day history of abdominal pain and nausea. Her doctor wrote that she was "very lethargic and looked cadaverous."

She presented with the typical appearance of lipodystrophia progressiva with the so-called "death's head" and circumoral wrinkling on speaking or smiling. Loss of subcutaneous fat was symmetrical and complete down to the pelvic girdle, where there was an abrupt change. Below this level subcutaneous fat was present in normal but not excessive amounts. Her weight was 3 st. 10 lb. 4 oz. (24.2 kg.). Examination was otherwise negative. In view of the recent illness further investigations were done: a Mantoux test, which was negative; E.S.R., 4 mm. in the first hour; Hb, 98%; W.B.C., 5,000; and *x*-ray examination of the chest, normal. No investigation of the urinary system was done at this time except for a routine examination of the urine, which contained no abnormal constituents. The mother was told that improvement in the child's appearance was unlikely, but that she would remain healthy.

In September, 1951, fifteen months later, the mother, anxious for something to be done to improve the child's appearance, took her to a London teaching hospital, where she was an in-patient for fifteen days. In the case summary on her discharge it was noted that the child "was said to be rather thirsty." The glucose-tolerance test was normal. No special urinary-tract investigations were done. It was concluded that she was "a case of lipodystrophia progressiva unassociated with evident endocrine disorder."

In February, 1952, four months later, the child was admitted to Bromley Hospital with a history of repeated vomiting for five days, and abdominal pain and red urine for three days. The temperature at the onset had been 103° F. (39.4° C.) and there had been repeated rigors, dysuria, and frequency. On examination she showed the features of lipodystrophy unchanged from when she was first seen twenty months previously. The child now looked toxic and dehydrated, with a dry furred tongue. The pulse was of poor quality and the rate 100 before admission. In hospital the rate was at first about 90, later rising on occasion to over 120. The temperature settled to 99° F. (37.2° C.) and for the next three weeks there was a low-grade pyrexia up to 99.5° F. (37.5° C.). During the fourth

week the temperature fell and was normal for the remaining three weeks in hospital. For the first few days tenderness was present in the right loin. There was no tenderness in the left loin or over the bladder. The B.P. was 120/80, and, with the exception of the urine, the remainder of the physical examination was negative.

The urine on admission was scanty and contained a very heavy cloud of albumin. There were numerous red cells, pus cells, and isolated cellular casts. Catheter specimens of urine were sterile. Five days after admission the blood urea was 330 mg. per 100 ml.; W.B.C., 19,000, with 80% polymorphs; E.S.R., 25 mm. in the first hour.

Four days later the blood urea was still 320 mg. per 100 ml. and oliguria persisted. The Bull–Borsh regime was then started, and the blood urea fell to 183 mg. per 100 ml. after a further five days and in the next fortnight to 40 mg. per 100 ml. The child's condition improved with the fall in the blood urea. An intravenous pyelogram, when the blood urea had fallen to normal, showed bilateral hydrocalicosis, hydronephrosis, and hydroureter more marked on the right (Fig. 1). Cystoscopy showed no abnormality. The child was discharged from hospital on April 9, weighing 4 st. 6 lb. (28.1 kg.), and returned to school one month later.

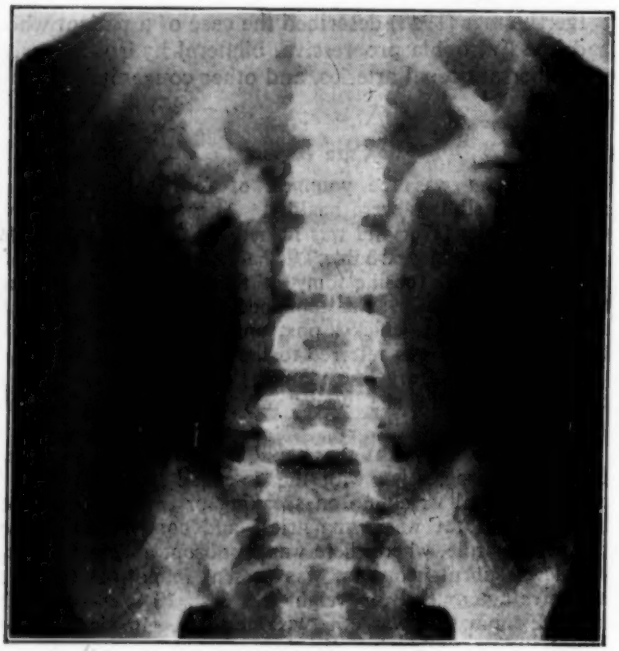

FIG. 1.—Intravenous pyelogram done on March 26, 1952.

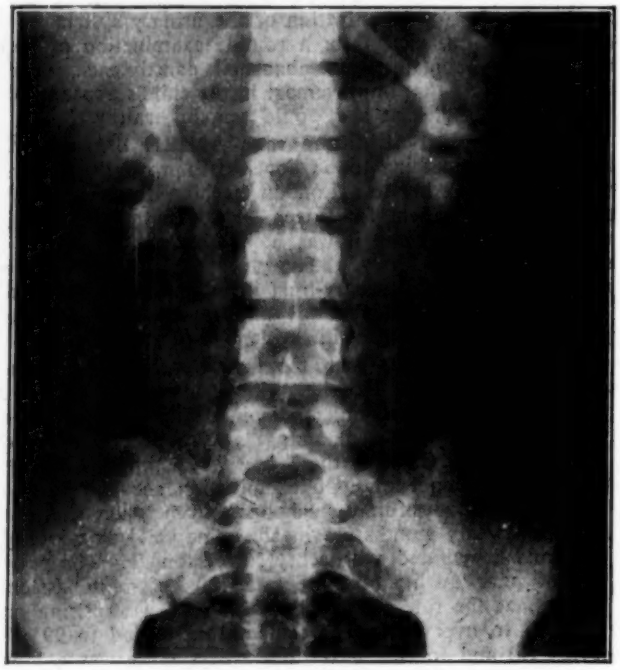

FIG. 2.—Intravenous pyelogram done on October 9, 1953.

During her stay in hospital there was striking mental instability, the child being one moment aggressive and abusive and the next exceedingly timid. This was in marked contrast to her mental state when her condition improved, her personality then becoming stable and pleasant. The mental changes appeared to be a manifestation of uraemia, improving as the blood urea fell.

When seen in the out-patient department three months later she was free of symptoms, was feeling well, and had won the high jump at school. No abnormal constituents were found in the urine, the intravenous pyelogram showed only slight bilateral hydronephrosis and hydroureter affecting mainly the right side.

Her progress was watched in the out-patient department and she continued to remain well until fourteen months later. While on holiday she was admitted on August 13, 1953, to the Royal County Hospital, Ryde, with a history of vomiting, abdominal pain, headache, and dark urine for four days. The urine contained large amounts of albumin, many pus cells, and red blood cells with a moderate amount of granular and cellular casts. The B.P. was 130/80, E.S.R. 47 mm. in the first hour, and Hb 90%. The blood urea was 73 mg. and later rose to 109 mg. per 100 ml. Before transfer back to Bromley Hospital the blood urea had fallen to 28 mg. An intravenous pyelogram (Fig. 2) showed little change from that done one year previously, but there was marked improvement as compared with the first *x*-ray films taken soon after the most severe uraemic episode. On discharge from hospital on October 12 she was free of symptoms and her general condition was satisfactory, although there was still a moderate albuminuria.

When seen in the out-patient department in March, 1954, she was feeling well. The B.P. was 140/80. The urine contained 0.5 g. of albumin and a moderate number of red cells and pus cells. The blood urea was 32 mg. per 100 ml. and the urea clearance (Van Slyke) 54%. An E.E.G. in November showed no abnormality.

Discussion

In retrospect, it appears likely that the first illness in June, 1950, was due to incipient or transitory uraemia and that she has therefore been in renal failure three times. The nature of the kidney trouble at 2½ years old is unknown.

Although the equanimity of most patients with lipodystrophy emphasizes their mental stability, psychological disturbances have occurred in a number of patients. Warin and Ingram (1950) reported two such cases and reviewed other instances of this association. The presence with lipodystrophy of mental disorder due to organic disease of the brain lends some support to the theory that this disease results from a lesion in the central nervous system. In our patient the mental changes were due to uraemia, and, although in none of the case reports was mental change attributed to this cause, renal and other organic disease may pass unrecognized when presenting with mental symptoms (Stokes *et al.*, 1954).

In this child the three attacks of uraemia were clearly due to the hydronephrosis. The cause of the uraemia in the patients with lipodystrophy described by Horton and Emmett (1932) and Berger (1932) was obscure. In Berger's patient it seems improbable that an acute exacerbation of chronic nephritis had caused uraemia when seven years later the patient was in good health and the blood urea 21 mg. per 100 ml. Intravenous pyelography, which might have shown a hydronephrosis, was not done in either of these two patients. This technique had not been introduced at the time Gerhartz (1916) and Klien (1921) described their cases.

Renal failure did not occur in Igersheimer's (1948) patient with lipodystrophy and hydronephrosis. Igersheimer maintained that lipodystrophy is due to a defect of the mesenchyme and described various mesenchymal abnormalities in his patient. He reviewed other published cases to support his view. The hydronephrosis in his patient was believed to be due to an aberrant renal artery. This was found at operation and cut. A subsequent intravenous pyelogram showed no change from the appearance before operation.

Igersheimer summarily dismisses the nervous, endocrine, and other causes suggested for lipodystrophia progressiva. The different hypotheses concerning aetiology have been fairly reviewed by Ellis (1951). There is much evidence to suggest that lipodystrophy may result from a lesion in the central nervous system (Warin and Ingram, 1950).

Besides that of associated mesenchymal defects or mere chance, there is another possible explanation for the occurrence together of uraemia and lipodystrophy. Lesions of two closely related areas of the brain, anterior to the hypothalamus, may be responsible for trophic changes and uraemia, both of these effects occurring if both areas are involved. Evidence that the cause of lipodystrophy may lie in a lesion related to the hypothalamus is found in the diencephalic syndrome (Russell, 1951), where profound wasting is a prominent feature. In Tizard's patient (1954) the profound wasting was a true lipodystrophy with disappearance of subcutaneous fat and no muscle-wasting. Dr. Russell, who saw this child, thought it likely that she had a diencephalic lesion. Evidence that trophic changes and uraemia can be due to lesions in closely related areas anterior to the hypothalamus is furnished by McLardy (1950). After prefrontal leucotomy, trophic changes with gross wasting and uraemia have often been described. These complications of the operation usually occur when the incisions go too far back (Freeman, 1953). McLardy has shown that prefrontal leucotomy can be followed by uraemia or trophic changes, depending upon which of two areas is damaged. Injury to posterior area 47 of the orbital cortex leads to uraemic death, and the severance of connexions between the caudate nucleus and Brodmann's (non-granular) cortical areas 8 and 6 is concerned with the trophic fatalities. The immediate cause of renal failure in McLardy's series of uraemic deaths is not known, but he mentions the work of Cort, who claimed to reproduce Trueta's renal shunt mechanism in cats by electrical stimulation of the cortex of area 13.

If renal failure in lipodystrophy is due to a lesion in the central nervous system, this could be caused by abnormal function of the autonomic innervation of the urinary tract, producing hydronephrosis, or of renal cortical arterioles, producing a Trueta shunt effect. Besides the evidence of the present case, hydronephrosis as a functional disorder of the urinary tract is common in man. The rare cortical necrosis of the kidney during pregnancy is the only disease which may be comparable to Trueta's shunt mechanism in the experimental animal.

Lesions affecting autonomic centres are responsible for diverse vegetative effects, including uraemia. The common idiopathic hydronephrosis with no organic obstruction may be due to disease of the central nervous system involving an autonomic centre regulating the function of the renal tract.

Summary

A case of lipodystrophia progressiva, temporary hydronephrosis, and recurrent uraemia is described.

The occurrence of renal disease with lipodystrophy is reviewed. The association of the two diseases may be fortuitous; the result of a mesenchymal defect; or the result of a lesion of adjacent centres in the central nervous system, responsible for the renal and trophic changes.

Evidence is submitted that a lesion anterior to the hypothalamus may be responsible for these changes.

My thanks are due to Dr. N. S. Plummer for permission to publish this case and for his helpful criticism.

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MALIGNANT GRANULOMA OF THE NOSE

BY

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The condition known as malignant granuloma of the nose is uncommon and almost invariably fatal. The chief purpose of this report is to present a unique result —a treated case which has remained healed for over five years. The secondary purpose is to present another case of a different and unusual type.

Only five cases of recovery appear in the literature, but closer examination of the case records and subsequent history reveals inconsistencies. Woods's case (1921) healed locally after interstitial irradiation, but the patient died within two years, of generalized sarcomatosis. The diagnosis of the original lesion must therefore be suspect. In the case of M'Arthur and Dew (1925) the local lesion healed after three doses of deep *x* rays, but the patient died four years after the last dose from what was called "miner's phthisis." No necropsy was permitted, and Stewart (1933) quotes a letter from M'Arthur in which the possibility of pulmonary sarcomatosis was envisaged. Schütz (1938) records eight cases, in one of which spontaneous resolution occurred, but the account is too brief to be entirely acceptable. Hoover (1941) describes an admittedly atypical case which apparently healed after excision of the granulomatous area followed by antisyphilitic treatment.

An exhaustive survey of the literature by Williams (1949) failed to reveal any cases of survival other than those cited above. His discussion of the pathology is most instructive, particularly in assessing a link with periarteritis nodosa and with certain types of hypersensitivity reactions. Following upon this paper, Williams and Hochfilzer (1950), Moore *et al.* (1951), and Woodburn and Harris (1951) have had some success with cortisone and A.C.T.H., but the follow-up period recorded is too short for appraisal.

Finally, Sneddon and Colquhoun (1952) claim a cure with chlortetracycline ("aureomycin") and chloramphenicol, but the patient died a year or so later, and, furthermore, the precise nature of the lesion was never identified by biopsy. They considered the lesion to be staphylococcal in origin, but no other case has been recorded in which the local lesion healed with antibiotics (Breckenridge *et al.*, 1954).

Case 1

A married woman aged 28 was first seen at the Royal National Throat, Nose, and Ear Hospital on June 24, 1947, complaining of right-sided nasal obstruction, an intermittent swelling in the right nasal cavity, a purulent nasal discharge, and considerable crusting with fetor. Some of the symptoms had been present for over two years. There was a large septal perforation, crusts in both nasal cavities, mucopus in the nasopharynx, and a nodular swelling of the right side of the palate. A radiographic opacity of the right antrum was present and antral lavage revealed pus and crusts. The W.R. was negative. On a tentative diagnosis of atrophic rhinitis, she was advised to use an alkaline nasal douche and a nasal paint of glycerin and glucose, night and morning, and this kept her relatively comfortable. As this diagnosis was not convincing, she was kept under close observation, attending frequently at short intervals, until on October 7 a large piece of necrotic bone, thought to be a sequestrum of the septum, was removed from the left side of the nose.

A few weeks later she was admitted to a hospital nearer her home because of acute maxillary sinusitis. This recurred three times during the next fifteen months, necessitating her readmission on each occasion. These attacks were treated with penicillin and antral lavage, and in September, 1948, by a Caldwell–Luc operation on the right side. After this operation the right side of the nose and the tissues underlying it literally melted away, and an ulcer appeared which rapidly spread upwards almost to the margin of the right orbit. At this stage I saw her again, quite fortuitously, in my out-patient clinic at another hospital, where she was referred by her doctor. It was now evident that this ulcer was the external opening of a large fistula into the right nasal cavity, right ethmoidal region, and right antrum, and that its margins consisted of necrotic bone and of granulation tissue (Fig. 1). The mucosa on the buccal surface of the palate was thickened and nodular, although still intact (Fig. 2), but on palpation it was found that the bone of the hard palate had been almost completely destroyed. A diagnosis of malignant granuloma now sprang to mind, and, so far as confirmation is possible, this diagnosis was confirmed by biopsies from the edge of the ulcer and from the swelling on the palate.

FIG. 1.—Case 1. Showing the external extent of the ulcer with necrotic bone in the margins.

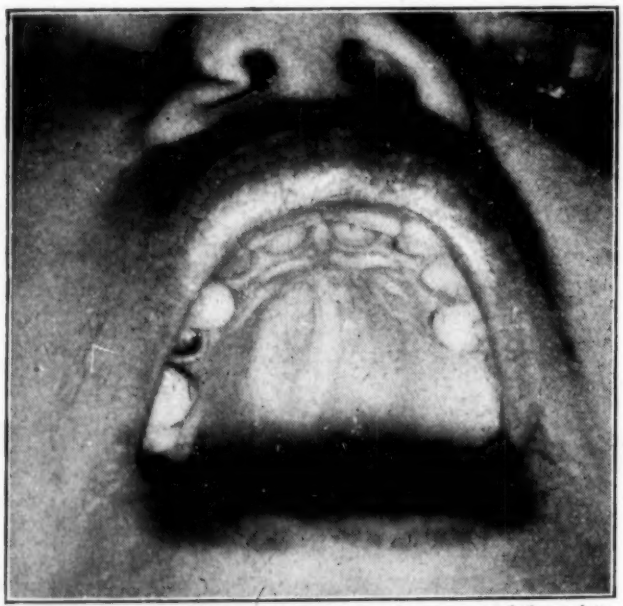

FIG. 2.—Case 1. Showing the nodular enlargement of the palate.

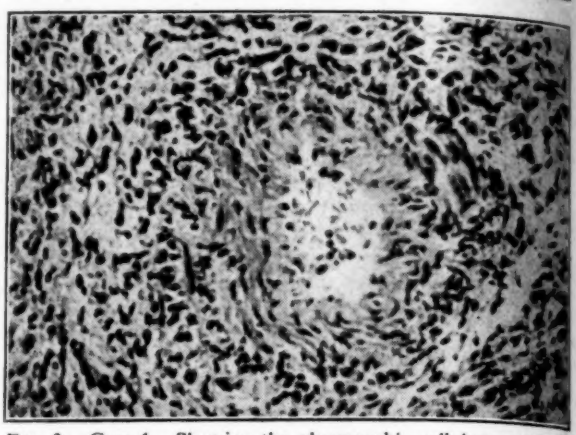

FIG. 3.—Case 1. Showing the pleomorphic cellular reaction and the absence of focal necrosis and of necrotizing angiitis. (×230.)

Dr. I. Friedmann's report is as follows: "The histological appearances (Fig. 3) of this case are characteristic of malignant granuloma of the nose in so far as they consist of a chronic fibrous non-specific inflammatory granulation tissue infiltrated by pleomorphic inflammatory cells, including plasmacytes and lymphocytes. There are no giant cells present and there is no evidence of focal necrosis, frequently seen in similar cases. A small artery found in the biopsy specimen shows no evidence of necrotizing angiitis. This histological picture virtually excludes all known forms of specific granulomatous reactions as well as neoplasm. There are possibly several histological types or variations of malignant granuloma of the nose. The most common type appears to be a pleomorphocellular granulation tissue as described in this case. In other cases one or more of the following morphological features have predominated: (1) histiocytes, (2) foreign-body giant cells, (3) extensive necrosis. One particular variety, the giant-cell granuloma, is frequently associated with necrotizing vascular disease resembling polyarteritis nodosa. The case here described appears to belong to the classical type as there was no sign of systemic vascular complications."

In spite of treatment with sulphonamides and penicillin, pieces of necrotic bone were daily extruded from the depths of the cavity, and later the palatal mucosa gave way. The patient was referred to Dr. M. Lederman, radiotherapist at the Royal Marsden Hospital, for irradiation, but after consultation it was decided not to risk a form of treatment which might itself cause bone necrosis. Large doses of potassium iodide together with a course of calciferol were given and the ulcer became cleaner and showed signs of healing. The horrible fetor disappeared and the steady necrosis and sloughing ceased. However, the improvement

was only temporary, and a few months later the condition again became noticeably active. Dr. Lederman then consented, with some misgivings, to try a course of deep *x* rays, and the very small dose of 300 r was administered between December 19, 1949, and January 21, 1950. A dramatic change followed. The margins of the ulcer became clean and a healthy skin–mucosal junction formed. The mucosal junction between the oral and nasal surfaces of the palate also healed. By April 12 there was no further evidence of activity, and the vast, hideous cavity gradually became lined with pink mucosa.

As the ulcer remained soundly healed, Mr. J. P. Reidy, early in 1952, began the difficult plastic reconstruction which is still in progress. In spite of four operations on the tissues of the nose and face, there has been no evidence of any return of the disease.

Comment

The natural history of malignant granuloma of the nose has not been precisely identified, and the histological picture itself has not been clearly established as a specific entity. Stewart's exhaustive review of the cases described up to 1930 was accompanied by a composite clinical description based on these records, but it is more than possible that some of them would not now be accepted as true cases of the disease. The lesion usually begins as an intranasal ulcerative process which soon appears on the face after having eroded the lateral wall of the nose or the anterior wall of the antrum. The facial tissues are progressively destroyed and bone necrosis with sequestration is a marked feature. The spread towards the pharynx is slower. Death usually results from cachexia, in anything from one to three years. The case reported here has followed the classical course, except for the end-result.

However, there is occasionally another type of case in which the necrotizing reaction remains confined within the nasal cavities and spreads over the surface of the mucosa. One such case has recently come under my care.

Case 2

A man aged 48 was first seen on October 26, 1954, complaining of pain in the nose for about four months. This pain followed a thyroidectomy. The teeth were thought to be the cause of the pain and had been extracted, but without relief. The right nasal cavity contained pus and crusts, and pus was found on antral lavage. On November 11 a granular area was noticed on the septum and a portion was removed for biopsy. This revealed a non-specific type of granulation tissue covered with a thick stratified squamous epithelium. The granular area increased in extent and a large ulcer appeared on the septum and also on the middle turbinal. On December 15 the patient was admitted and the antrum opened and inspected by the Caldwell–Luc approach. Macroscopically it appeared normal, and pieces of tissue for biopsy were taken from the antral mucosa, the right middle turbinal, and the septum. The antral mucosa was normal, but (Fig. 4) "the nasal mucosa is densely infiltrated by large lymphocytes and histiocytes showing considerable irregularity of nuclear size and shape. There are numerous plasmacytes present, and frequent mitoses are seen. The cartilage of the nasal septum has been eroded by the process" (Dr. I. Friedmann). Dr. L. W. Pagel concurred with this description, and both pathologists agree that this is a case of malignant granuloma. The distinctive feature of predominance of histiocytes and plasmacytes is a variation to which Dr. Friedmann has already drawn attention.

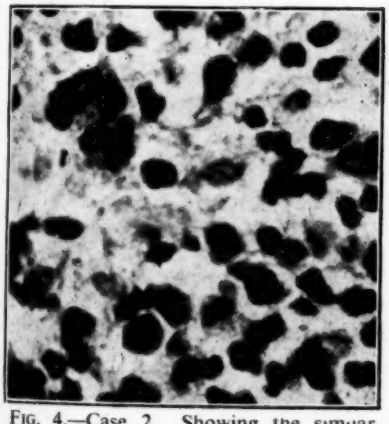

FIG. 4.—Case 2. Showing the similar pleomorphic reaction, but with an excess of histiocytes and plasmacytes. (×750.)

By January 8, 1955, destruction of the septum had occurred, but the process, although spreading rapidly within the nasal cavity, still shows no sign of involving the skin.

Discussion

Although it is possible that these two differing clinical pictures are associated with certain variations in the histological picture (Friedmann, 1955), the ultimate prognosis has hitherto been fatal in both types of case. Case 2 has been treated in a similar manner to Case 1, but it is as yet too early to say what will happen.

No rationale is claimed for the treatment given in Case 1, much less for the dramatic success with which it was attended. It was frankly a shot in the dark, entirely on an empirical basis of trial and error. The patient is apparently cured, presumably by the irradiation, as resolution followed immediately after it was given, and the disease had previously resisted, or relapsed after, other methods of treatment. The reluctance in trying irradiation naturally follows the knowledge that irradiation can itself cause, especially in bone, a similar necrotizing type of lesion. The end-result indicates that an almost absurdly small dose was the treatment of choice in this particular case, and would be well worth trying in other similar cases. In fact, at a meeting of the Section of Laryngology of the Royal Society of Medicine on December 3, 1954, Mr. Gilroy Glass reported two cases which were treated similarly and which have responded similarly. They had remained healed for about a year, up to the time of his report.

Summary

A case of malignant granuloma of the nose is described which has been cured by a very small dose of deep *x* rays. This is the first genuine case recorded in which the patient has not died of the disease.

In addition to the classical type of case with sloughing of the facial tissues there is another type which remains confined within the nasal cavities, spreading superficially in the mucosa.

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The third pamphlet in a series on Food Hygiene has just been published by the Central Council for Health Education. This leaflet deals with refrigerator storage. It describes how the refrigerator should be used and cleaned, and what foods should have priority in it. A previous leaflet advised on food storage without a refrigerator, and another presented a "Shopping Quiz" for housewives, drawing attention to poor hygiene standards in food shops.

IMMEDIATE PARTIAL GASTRECTOMY FOR PERFORATED PEPTIC ULCER

BY

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Between March, 1950, and December, 1951, five elective partial gastrectomies were performed at the University Surgical Unit for severe recurrent symptoms following simple closure of a perforated peptic ulcer. The simple closure antedated the ultimate resection by periods varying from six months to three years. Impressed with the inconvenience to the patients of disabling symptoms in the intervening period and of the increased technical difficulties at the time of the second operation, it was decided to treat certain selected cases of perforated peptic ulcers by immediate partial gastrectomy.

Some would consider that the treatment of a perforated peptic ulcer is a life-saving measure and that the simplest operation is all that should be attempted. Figures from Continental clinics support the contention that immediate gastrectomy is a safe procedure. Nuboer (1951) published a series of 131 immediate partial gastrectomies for perforated peptic ulcer with a mortality of 3.8%. Very low mortality rates are also revealed by certain Russian authors (Rozanov, 1953; Lidskii and Nurenberg-Charbiani, 1953). Lowdon (1952) performed partial gastrectomy without mortality in 51 consecutive cases of perforated peptic ulcer in patients between the ages of 20 and 70. These figures imply that in experienced hands the mortality rate from immediate partial resection can be expected to be no greater than that of simple suture.

The issue over which the various exponents of the major procedure are at variance is in the selection of the cases. In Nuboer's clinic "since 1943 partial gastrectomy has been done in nearly all cases of perforated ulcers. No regard is paid to the patients' age or duration of perforation." Nuboer justified this apparent lack of discrimination by suggesting on histological evidence that all the perforations, even in patients with a short history, were of a chronic nature. These findings, however, were not confirmed by Lowdon (1952) in some of his cases with a history of short duration. Forty (1951) quoted findings in 19 perforations examined histologically, in which no fewer than 15 were classified as being of an acute nature, and such findings imply that a critical assessment of each individual case is desirable. It would appear reasonable, therefore, to select individuals for immediate partial gastrectomy by estimating their probable pronosis after simple suture alone, the items of importance in such assessment being (*a*) the situation, appearance, and size of the perforation, (*b*) the duration and severity of the symptomatology prior to perforation, and (*c*) an appreciation of the statistical surveys of progress after peptic ulcer perforation.

Results

Between January, 1952, and June, 1954, 54 cases of perforated peptic ulcer were admitted under our care: 4 were treated conservatively with 2 deaths; 2 elderly patients with perforated gastric ulcer found to be unfit for resection were treated by simple suture, with 1 death; and 33 cases of perforated duodenal ulcer were treated by simple closure, with 3 deaths.

The following brief summaries describe the remaining 15 cases, which were treated by immediate partial gastrectomy:

Case 1.—Male, aged 65, with a two-year history of dyspepsia, perforated 16 hours before admission. Large perforation of duodenum with gross peritoneal soiling. Immediate partial gastrectomy; uneventful recovery.

Case 2.—Male, aged 60, with a long history of dyspepsia, perforated two hours before admission. Large perforation of anterior wall of first part of duodenum. Immediate partial gastrectomy; uneventful recovery.

Case 3.—Male, aged 55, with recent symptoms, perforated seven hours before admission. General condition poor. Perforated lesion found on distal third of greater curvature of stomach. Partial gastrectomy; developed paralytic ileus and renal failure; died on 11th post-operative day. Histology—benign gastric ulcer.

Case 4.—Male, aged 66, with recent dyspepsia and melaena, perforated 8 hours before admission. Perforation of anterior wall of stomach, with considerable peritoneal soiling. Immediate gastrectomy; general peritonitis and paralytic ileus; died on 10th post-operative day. Histology—chronic gastric ulcer.

Case 5.—Male, aged 64, with a long dyspeptic history, perforated six hours before admission. Large perforated duodenal ulcer, with gross peritoneal soiling; immediate gastrectomy; uneventful recovery.

Case 6.—Male, aged 64, with a four-year history of severe dyspepsia, perforated 15 hours before admission. Large perforation of pyloric antrum with early localization; uneventful recovery followed partial gastrectomy. Histology—gastric carcinoma.

Case 7.—Male, aged 60; previous gastro-enterostomy in 1933, perforated three hours before admission. Large perforated lesion just above the previous anastomosis seen at operation. Immediate gastrectomy; uneventful recovery. Histology—gastric carcinoma.

Case 8.—Male, aged 56; continuous dyspepsia since a previous perforation was successfully sutured in 1943. Perforated duodenal ulcer treated by immediate partial gastrectomy; uneventful recovery.

Case 9.—Male, aged 60, with a 20-years history of dyspepsia, perforated 12 hours before admission. Perforation in a stenosed duodenum treated by immediate gastrectomy; uneventful recovery.

Case 10.—Male, aged 42, with a history of two previous perforations, was admitted four hours after his third. Perforated duodenal ulcer treated by immediate gastrectomy; uneventful recovery.

Case 11.—Male, aged 71, with a 25-years history of dyspepsia, presented with a perforation and haematemesis. Partial gastrectomy for a large perforated duodenal ulcer; uneventful recovery.

Case 12.—Male, aged 56; long history; perforated eight hours before admission. Immediate partial gastrectomy performed in presence of perforated and stenosed duodenum; uneventful recovery.

Case 13.—Male, aged 44; eight years' dyspepsia, perforated three hours before admission. Perforated lesion of lesser curve dealt with by a Pauchet type of partial gastrectomy; uneventful recovery. Histology—chronic gastric ulcer.

Case 14.—Male, aged 59; recent symptoms. Large perforation of duodenum treated by partial gastrectomy five hours after onset of symptoms; uneventful recovery.

Case 15.—Male, aged 70, perforated three hours before admission. Very large perforation of duodenum treated by partial gastrectomy. Satisfactory recovery followed resuture of a wound dehiscence on the seventh post-operative day.

Discussion

If the patient's general condition permits, a partial resection is the operation of choice in nearly all cases of perforated gastric ulcer. Such perforations, especially if chronic, are often difficult to suture, the amount of intraperitoneal contamination is great, and containment of the infective material is unsatisfactory. The greater mortality following treatment by simple suture and toilet of patients with perforated gastric as compared with duodenal ulcers has been demonstrated by Chamberlain (1951) and Gilmour (1953). Another justification for routine immediate resection is the high proportion of carcinomas of the stomach which appear in the guise of simple gastric perforation. Thus Doll (1950) quoted 17 cases of perforated carcinoma of the stomach occurring in the eleven years 1938–48 in the Central Middlesex Hospital. Perforations were found at operation in 11 cases, but only 3 were recognized to be neoplastic, and 7 were discharged from hospital with the diagnosis of simple gastric ulcer. Kennedy (1951) quoted a five-year series of 111 acute perforations from the London Hospital which included seven cases of perforated gastric carcinoma. In the present series Cases 6 and 7, thought at operation to be of a simple nature, proved on histological examination to be malignant.

In the case of perforated duodenal ulcers the possibility of neoplasm is so rare as to be disregarded. The size of the ulcer, however, should be considered when deciding on the procedure to adopt. Simple closure is unwise where considerable cicatricial narrowing is present or in cases of large perforation, as simple closure may produce complete stenosis. The occlusion of a large duodenal perforation by an omental plug, although perhaps immediately successful, leaves an area of very imperfectly constituted duodenal wall which, in the continued presence of hyperchlorhydria, will inevitably re-ulcerate and perhaps re-perforate. Luer (1949) found that if the perforation was 1 cm. in diameter or more, the mortality rate following simple suture was more than double the rate in smaller perforations. The experience in this small series of cases suggests that radical operation in such emergency cases is no more difficult than in elective cases and that the subsequent smooth post-operative course is most satisfactory.

A history of previous perforation was taken as an indication for gastric resection if the case was in other respects satisfactory (Cases 8 and 10).

In either gastric or duodenal perforations the co-existence of haemorrhage increases the mortality rate (Avery Jones *et al.*, 1950). This dangerous combination is most satisfactorily dealt with by immediate partial gastrectomy, and in the present series was regarded as a definite indication if the patient's general condition allowed (Case 11).

The appearance of chronicity in a perforated duodenal ulcer may be simulated by inflammatory oedema, and in the absence of previous ulcer dyspepsia it may well be that the lesion is an acute one and immediate resection is unjustifiable : nor should duration of symptoms alone be taken as unequivocal evidence of chronicity. If the perforation is small, even with a long preceding period of dyspepsia, it may be, as contended by Forty (1951), that the patient has had a series of acute or subacute ulcers, each healing in turn. If, however, the perforation has the appearance of being in a chronic ulcer and the patient gives a well-defined period of disabling dyspepsia with perhaps previous hospital treatment and radiological confirmation of a chronic ulcer, immediate partial gastrectomy is justifiable.

The results of a follow-up study of 733 cases of perforation treated by simple suture are valuable in assessing the probable ultimate prognosis after perforation (Illingworth *et al.*, 1946). It was found that remission of ulcer symptoms after perforation was seldom of long duration, within five years 70% having relapsed and 50% developing severe symptoms. The prognosis was found to be worse in cases with a long antecedent history, whilst the incidence rate of major complications, particularly re-perforation and haematemesis, was 20% within five years of perforation.

When the series presented in this paper was started it was hoped that a critical selection of cases for immediate gastrectomy would eliminate the expected 20% of major complications and a proportion of the remaining cases which would be expected on the above statistical evidence to relapse. On making the selection we were influenced by the fact that the majority of patients seen in this hospital are industrial workers, miners, and others in whom the economic factor of loss of work is important and in whom prolonged dietary out-patient treatment is often impracticable.

In assessing fitness for immediate partial gastrectomy the patient's general condition was the main guide, and no arbitrary time interval since the onset of symptoms was laid down. For example, in Case 1, although the ulcer had perforated 16 hours previously, the patient was in excellent general condition and, following partial gastrectomy, made an uninterrupted recovery. A gross degree of peritoneal soiling was usually regarded as a contraindication to gastric resection, although in the first case in the series recovery followed gastrectomy in the presence of gross peritoneal contamination.

In no case did the technique of operation present any marked difficulty, and in general Nuboer's findings were confirmed. It was usually easy to free the duodenum, pylorus, and stomach from the inflamed and oedematous surrounding tissue. As Lowdon pointed out, the anterior duodenal perforation is usually unassociated with the technical difficulties so common with posterior and penetrating ulcers. In the majority of cases the closure of the duodenal stump was simple, although when dealing with perforated duodenal ulcers it was in most cases necessary to perform an open division and closure of the duodenum as the oedema of its walls and the size of the perforations prevented the application of a clamp distal to the ulcer. No case of leak from the duodenal stump occurred.

The two fatalities occurred early in the series, and in each case a considerable degree of peritoneal contamination accompanied the perforation. This subsequently led to a more cautious attitude in such cases, although an uneventful recovery followed immediate resection in Cases 1 and 5, in both of which peritoneal soiling was considerable. Tanner (1954) has reported similar successful cases of immediate gastrectomy performed in late perforation with frank pus in the peritoneal cavity.

The remaining cases all had a smooth post-operative recovery, the results encouraging us to continue the policy of performing immediate resection in selected cases.

Summary

Experience with immediate partial gastrectomy for perforated gastric duodenal lesions is recorded.

The operation was performed in carefully selected cases only.

The chief criteria for such selection in a patient fit for resection were (*a*) any perforated gastric lesion, (*b*) large perforations, (*c*) a history of previous perforation, (*d*) a long preceding history of ulcer dyspepsia, and (*e*) concomitant haematemesis.

Fifteen cases were selected for immediate gastrectomy in a series of 54 perforations dealt with over a period of 30 months. There were two fatalities.

The operation in no case presented any technical difficulty and the post-operative period was uneventful.

ADDENDUM.—Since June, 1954, a further 15 cases of perforated peptic ulcer have been admitted to the University

Surgical Unit. Four of these cases were dealt with by immediate partial gastrectomy without mortality.

We wish to thank Professor R. P. Jepson for his advice during the preparation of this short communication.

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CONGENITAL ATRESIA OF THE BILE DUCTS

REPORT OF CASE TREATED SUCCESSFULLY BY CHOLECYSTOJEJUNOSTOMY

BY

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John Thomson, of Edinburgh, first aroused interest in this condition by his careful analysis of 50 cases in 1892. Holmes (1916) collected 120 cases from the literature, described a large number of variations in malformations of the extrahepatic bile ducts, and concluded that about 16% of the patients could be amenable to surgical treatment. Ladd (1928) was the first surgeon to operate successfully upon a case of congenital atresia of the choledochus. Gray *et al.* (1948), in reporting two cases of their own which were successfully treated by cholecystogastrostomy, state that between 1928 and 1948 only 17 cases were recorded in the literature as being cured by surgical measures.

Durell and Halliwell (1952) described a case of congenital atresia of the common bile duct which was cured by cholecystogastrostomy, and remarked that surgical intervention had been successful apparently in only 21 cases up to 1949. Moore (1953) explored 31 cases of congenital atresia of the bile ducts and performed 8 anastomoses, only one of these patients surviving operation. Likewise, Greaney *et al.* (1954) explored 33 cases, 9 which were suitable for biliary-intestinal anastomosis, and 3 of which were cured. Gross (1953), in by far the largest series, records 146 cases: in 119 nothing could be done on abdominal exploration; in 27 the gall-bladder or the hepatic or common duct was available for anastomosis to the duodenum, and 12 of these were cured.

So far as can be ascertained from published articles, 38 cases of congenital atresia of the extrahepatic bile ducts have been successfully treated by surgery. The majority of the successful operations for this rare abnormality have been recorded by American surgeons. Durell and Halliwell (1952) gave an excellent account of the first case to be cured by cholecystogastrostomy in this country.

So far as I am aware the case described below is the first recorded account of a successful cholecystojejunostomy combined with jejunojejunostomy for atresia of the common bile duct to be published in the British literature.

Pathology

In this congenital abnormality one or more parts of the external biliary tract are either absent or exist as fibrous cords. The extent of such obliteration determines the operability of the case. It will be operable if the atresia exists in the lower portion of the hepatic duct or in the common duct, or if the gall-bladder and cystic duct communicate with the hepatic duct which is distended with bile.

The gall-bladder may be found in one of four pathological conditions: (1) it may be absent or atretic; (2) it may contain a small lumen which does not communicate with the ductal system; (3) it may be distended with white bile—mucocele; and (4) it may be normal or enlarged and contain normal bile, indicating that the blockage is in the common duct. The liver is enlarged, stained dark green, and diffusely nodular, portraying the picture of portal cirrhosis of the obstructive type. The edge of the spleen is usually palpable and portal hypertension is a common feature. Ascites may or may not be evident. Petechiae, extravasation of blood in the subcutaneous tissues, and cerebral haemorrhage have been observed in some of these cases.

Diagnosis

The clinical picture is similar in most cases. The outstanding sign is jaundice, which is present at birth or appears two or three weeks later. This is at first mild, the skin being merely tinted pale yellow, but gradually increases until at the end of a month or so it is intense and gives place to a greenish-yellow hue.

The congested cirrhotic liver at the same time gradually enlarges and feels unduly hard on palpation, its edge being rounded and firm. The notched margin of the spleen is frequently detected. The stools are white, putty-like in consistency, and acholic, while the urine is bile-laden and dark brown. It should be noted that the stools are always white from birth even though jaundice may not be noticed until the second or third week of life.

The icteric index varies in different infants and from day to day in the same patient, ranging mostly between 50 and 200; the blood picture shows a secondary anaemia; the red cells are not unduly fragile; there is no microspherocytosis; the clotting time is seldom elevated; the prothrombin time may be lowered; and the liver-function tests support a diagnosis of obstructive jaundice.

The condition may be confused with icterus neonatorum, erythroblastosis foetalis, jaundice of haemolytic sepsis, congenital syphilis, or congenital haemolytic anaemia. Every attempt should be made to arrive at a diagnosis within the first four or five weeks of life and not to delay exploratory laparotomy beyond the second month, as the majority of patients will die of liver failure within five months if the blockage is not relieved. It is a surprising fact, however, that a few patients possessing no extrahepatic ducts have lived to be 8 to 10 months old. The diagnosis can be arrived at by a process of elimination with a fair degree of certainty by the end of the first month of life, and sometimes earlier than this. In other words, the diagnosis is made by excluding other causes of jaundice and by proving that the infant under investigation is suffering from obstructive jaundice.

To-day, about 20 to 25% of these babies present conditions of the extrahepatic ducts which are correctable only by operative measures.

Operative Treatment

Pre-operative measures include the correction of dehydration, one or two small transfusions of blood, and the administration of vitamin K. Penicillin is given intramuscularly before and after operation.

The anaesthetic of choice is open ether. Satisfactory relaxation of the abdominal muscles cannot be obtained with local analgesia. The use of muscle relaxants is definitely contraindicated. There is a choice of two incisions: right

vertical epigastric muscle-split incision or Kocher's incision. Considerable difficulty may be experienced in determining the type of malformation present. The liver is enlarged and defies mobilization, the gall-bladder and the ducts (when present) are small, the anomalies show wide variations, and the operative field is highly vascular.

If the gall-bladder is present and the common bile duct cannot be seen, a wise manœuvre consists in inserting a hypodermic needle into the fundus of the viscus and distending the gall-bladder with saline solution. When the cystic duct is patent and the common duct is present the fluid will distend the choledochus and bring it into view. In some cases of obstructive jaundice the lower end of the common bile duct is plugged with mucus or inspissated bile, and this method may be sufficient to produce displacement of the mucus-laden biliary sand and cause it to pass into the duodenum, thus relieving the obstruction.

Some surgeons practise operative cholangiography with the object of illuminating the existing ductal system. I have no special experience of this method of investigation for the type of case under discussion. Where, however, there is a definite stenosis of the common bile duct, although cholecystogastrostomy has often been practised for the relief of this condition, Ladd and Gross (1941) have no doubt that choledochoduodenostomy, when feasible, is a far superior operation in spite of its greater technical difficulty. According to Gross (1953), choledochoduodenostomy or hepaticoduodenostomy is the operation of choice when the lower end of the common duct is atretic or when only a nubbin of the hepatic duct is available for anastomosis to the intestine. I believe, however, that the mobile proximal loop of jejunum is more suitable for end-to-side union to the bile duct or gall-bladder than is the thick-walled pyloric segment of the stomach or the tethered duodenum.

Choice of Operation

The choice will in many cases depend upon the site and extent of the obliterative process and also upon the condition of the gall-bladder itself (see Table).

Conditions and Appropriate Operations

Condition Found at Operation	Operation of Choice
A Gall-bladder present; cystic duct communicates with main ducts; stricture *lower end* of common bile duct	(1) Cholecystojejunostomy plus entero-anastomosis (2) Choledochoduodenostomy (3) Cholecystoduodenostomy (4) Cholecystogastrostomy
B Gall-bladder functionless or absent; stricture lower end of common bile duct	(1) Choledochoduodenostomy (2) Choledochojejunostomy plus entero-anastomosis
C Extensive stricture of common duct, but hepatic duct patent and contains bile	(1) Hepaticojejunostomy plus entero-anastomosis (2) Hepaticoduodenostomy
D No extrahepatic ducts	(1) Longmire's operation

When choledochoduodenostomy is a feasible procedure the bulbous lower end of the common duct should be freed and divided, and a small short rubber tube or a piece of No. 8 catheter about 1.5 cm. long should be inserted upward toward the hepatic duct. An opening is made in the antero-superior wall of the first part of the duodenum, opposite the end of the duct, and the small segment of catheter is led through the hole into the lumen of the bowel. With the tube in place, a single row of closely and carefully applied interrupted mattress sutures of fine silk or "deknatel," mounted on eyeless needles, is inserted so as to anchor the wall of the duct to the duodenum.

Hepaticoduodenostomy or hepaticojejunostomy is likewise performed with one row of interrupted mattress sutures, but after the latter operation an entero-anastomosis between the afferent and efferent limbs of the jejunum is carried out to divert the gastric and duodenal contents away from the vulnerable biliary tree.

When the gall-bladder obviously contains bile, as demonstrated by aspiration into a Record syringe, the organ may be anastomosed to the stomach, the duodenum, or to a loop of proximal jejunum with every hope of success. The operative technique of cholecystojejunostomy combined with jejunojejunostomy is described in the following report.

Case Report

The patient was a full-term male child born on October 8, 1951. He was normal at birth and weighed 7 lb. (3.2 kg.). Delivery was uneventful. The infant was breast-fed. Jaundice was noticed during the second week of life, the urine was dark brown, and the stools were white. No drugs had been administered. The parents and two other children were alive and well. There was no family history of jaundice, syphilis, or congenital deformity. The patient was admitted, under my care, to the Southend General Hospital.

On admission the infant was 1 month old and his weight 7 lb. 11 oz. (3.5 kg.). He was ill and apathetic, with jaundice of the skin and conjunctivae. No petechial haemorrhages or rashes could be seen, nor was there any evidence of sepsis of the skin or umbilicus. On inspection the abdomen was slightly protuberant and there were no distended veins. There was a moderate degree of hepatomegaly, as the rounded edge of the liver could be felt three fingerbreadths below the right costal margin. The spleen could not be palpated. A nystagmus was present, with no other abnormal neurological signs. The urine was a deep brown colour and contained bile salts and pigments. No urobilinogen was present. The stools were white and obviously contained no bile pigments. The value for haemoglobin was 5.6 g. per 100 ml. of blood (or 36%); the red cell count was 2,300,000; the colour index was 0.8; and leucocytes numbered 13,000 per c.mm. Red blood cells were of normal fragility, and 20 nucleated red cells were seen while counting 100 white cells.

The Wassermann and Kahn reactions were negative. The van den Bergh test gave a direct positive reaction and the serum bilirubin was 10.3 mg. per 100 ml. Blood grouping showed that parents and baby belonged to Group A and Rh positive.

A diagnosis of congenital atresia of the bile ducts was made. The infant's general condition was improved by two intravenous infusions of 120 ml. of blood, which raised the haemoglobin to 80%, and by the intramuscular administration of vitamins B and K.

Four days after admission to hospital the child's condition deteriorated, opisthotonos developed, and the nystagmus increased. The condition was diagnosed as an intracranial haemorrhage, and lumbar and ventricular punctures were performed. No cerebrospinal fluid was obtained on lumbar puncture and the ventricular fluid contained blood. The ventricular tap was repeated two days later and the fluid was blood-stained and xanthochromic. Six days later the circumference of the head had increased and bulging of the anterior fontanelle was present. The subdural spaces in each side were explored and 4 ml. of dark-brown blood was removed from the right side. As no further haemorrhages occurred, operation was carried out, under ether anaesthesia, on November 29, 1951.

Operation.—The abdomen was explored through a vertical right epigastric muscle-split incision which extended from the costal margin to 1 inch (2.5 cm.) below the umbilicus. Exposure revealed an enlarged cirrhotic dark-green liver. The spleen was larger and firmer than normal and a small amount of yellowish ascitic fluid was removed by aspiration. The tiny gall-bladder was tensely distended and the common bile duct ended in a bulbous nubbin above the duodenum. A hypodermic needle was inserted into the fundus of the gall-bladder and yellow bile was aspirated into a Record syringe, after which saline solution was forcibly injected to distend the minute ducts. The common bile duct ended abruptly about 2 or 3 mm. below the point

of entrance of the cystic duct. The fundus of the gall-bladder was mobilized; a long loop of the proximal jejunum was drawn upward in front of the transverse colon; and the apex of the loop was anastomosed to the full length of the gall-bladder by the side-to-side method, using two rows of interrupted sutures of the finest silk, mounted on eyeless needles. Portions of the jejunum proximal and distal to the stoma were anchored to the capsule of the liver to relieve any tension on the suture line. The operation was completed by performing a side-to-side jejunojejunostomy, well below the previous anastomosis, with the object of diverting gastric and intestinal contents from the biliary tree. The individual layers of the abdominal incision were approximated with interrupted sutures of silk, and a small dressing was strapped over the wound.

Post-operative Progress.—Bile was noticed in the vomitus the night after the operation and in the stools three days later. During the next week the jaundice began to fade and the urine became lighter in colour. The liver was not palpable three weeks after operation. The wound healed soundly, jaundice entirely disappeared, no further haemorrhages occurred, the appetite rapidly improved, and the infant made an uninterrupted recovery. He was discharged from hospital six weeks after operation, weighing 9 lb. 2 oz. (4.1 kg.). The patient has been examined periodically during the last three years. When last seen he looked the picture of health and was developing normally.

Conclusions and Summary

A newborn child who has jaundice should be subjected to an exploratory operation shortly after a diagnosis of *obstructive* jaundice is made.

A search then must be made for any evidence of extrahepatic biliary passages which might be used to establish a free flow of bile into the intestinal tract.

Fully 20% of cases of atresia of the bile ducts can be cured by the performance of choledochoenterostomy or cholecystoenterostomy.

The techniques of these operations are briefly discussed.

A case of congenital atresia of the common bile duct, which was successfully treated by cholecystojejunostomy combined with entero-anastomosis, is described.

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Ambulance, a professional journal for ambulance and industrial first-aid personnel, has had its first issue. A development of the quarterly review published by the Institute of Certified Ambulance Personnel for their members, *Ambulance* is expected, while continuing to be the official organ of the Institute, to interest readers outside it. It will be on sale to the public (price 1s.) and be produced four times a year. Its aim is to encourage free expression of ideas, even if these do not represent the official views of the Institute, and its columns are open to any reader for discussion on any topic which concerns ambulance men and women. The theme of the first issue is industrial safety. An editorial suggests that "the first-aid arrangements made by industrial firms under the Factory Acts are capable of improvement if they are to safeguard workers under present-day conditions." Another article discusses the prospect of an industrial medical service being set up.

ATTEMPTED SUICIDE WITH METHYLPENTYNOL AND PERSOMNIA

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Methylpentynol ("oblivon") is an unsaturated tertiary carbinol described by Margolin *et al.* in 1951. "Persomnia" is a synergistic combination of the open-chain ureides, carbromal and bromvaletone. Both these drugs have sedative and hypnotic powers, and, as well as being prescribed widely, are freely obtainable without prescription. The following case is described because there are still relatively few reports of overdosage with methylpentynol, and because this is the first reported case of attempted suicide with this combination of drugs.

Case Report

A soldier aged 38, weight 140 lb. (63.5 kg.), attempted suicide on February 6, 1955, by swallowing 25 capsules of oblivon (6.25 g. of methylpentynol) and about 75 tablets of persomnia (225 gr. (15 g.) of carbromal and 75 gr. (5 g.) of bromvaletone). These drugs were purchased from chemists' shops without prescription. The man was suffering from a severe reactive depression of two weeks' duration.

At 11.30 p.m. he began his attempt by taking oblivon, and continued with persomnia until he fell asleep. At 7.30 a.m. the following morning he was discovered unconscious on his bed, and tablets were found on the floor and in the bed. He was unresponsive to any stimuli. When seen by a medical officer at 8 a.m. he was in coma, and was at once transferred to hospital.

On admission at 9 a.m. he was found to be still comatose, but his colour, breathing, and pulse volume were satisfactory. Gastric lavage with sodium bicarbonate solution was performed and 20 mg. of amphetamine sulphate was left in the stomach. General supportive therapy was begun and he was started on intramuscular amphetamine. By 1.30 p.m. his coma had lightened, and by the following morning he was fully conscious. He was unable to recall anything from the time he took the drugs until he awoke in hospital on February 8. He was quite rational and was able to give a coherent account of himself. His only complaint was of headache. There was slight pyrexia, which was accounted for by bronchitis due to secondary respiratory infection. On February 11 he complained of pain in the left popliteal fossa, and this was found to be due to early thrombophlebitis.

The next day he was transferred to the psychiatric division of the Royal Victoria Hospital. The thrombophlebitis and residual bronchitis cleared up with penicillin. There was no apathy or ataxia, and he was left with only some depression relevant to his problems. During the next month he improved with sedation and psychotherapy.

Comment

Bourne (1954) and Lemere (1952) have reported cases of overdosage by methylpentynol, with recovery, in patients who had ingested respectively 6.25 g. and 8.75 g. The largest recorded overdose followed by recovery was 10 g. (Brown and Ellis, 1955). The only reported fatality appears to have followed a dose of 4.5 to 6 g. (Cares *et al.*, 1953).

Only one case of death from persomnia has been recorded (Coroner's Court, Bedford, 1952). This occurred in a woman

who swallowed over 200 tablets—800 gr. (52 g.). Hobart (1951) states that detoxication of the open-chain ureide sedatives is fairly rapid, and that 60–600 gr. (4–40 g.) have been taken in suicidal cases without harm.

Synergism between methylpentynol and barbiturates resulted in death in a man who took 9 oblivon capsules and 20 pentobarbitone sodium ("nembutal") tablets (*British Medical Journal*, 1955). Although it appears from our case that methylpentynol and persomnia do not potentiate each other, the possibility of an additive effect might be considered.

Finally, we would agree with Glatt (1955), who said with reference to methylpentynol, "It is regrettable that members of the public should still be able to purchase large quantities of this drug so easily without a prescription, in spite of the advice of the Pharmaceutical Society; it should be supplied only on a prescription." On the other hand, there are no indications for placing special restrictions on the sale of persomnia, but note should be taken of a recent report in the English literature of a purpuric eruption caused by carbromal (Borrie, 1955).

Summary

A soldier aged 38 attempted suicide by swallowing 25 capsules of oblivon and 75 tablets of persomnia. He was suffering from reactive depression. He recovered on routine treatment. This is the first reported case of attempted suicide with this combination of drugs.

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Medical Memoranda

Recurrent Abortion Associated with a Bicornuate Uterus

A successful outcome to a pregnancy in one horn of a bicornuate uterus is by no means a rarity, but the problem of how best to advise a patient with such a developmental abnormality of the uterus after four successive abortions may be difficult to solve. This is illustrated by the following case.

Case Report

When first seen by me at Farnborough Hospital in 1949 the patient was a healthy woman aged 28. Her general medical and family history contained no features of relevance. Menstruation had begun at 15, and periods of six days' duration were occurring regularly at 26-day intervals. Her first four pregnancies all terminated in abortion, and the details may be summarized as follows.

The first pregnancy, in 1943, ended in abortion at two months and was followed by evacuation of the uterus under general anaesthesia. A diagnosis of "subseptate uterus" was made, but a hysterogram some six months later was reported as "indefinite," as the dye was not retained.

The second pregnancy, in 1946, terminated in abortion at 10 weeks. The patient was receiving weekly injections thought to have been of progesterone, and it was on the day after the third of these that the abortion occurred.

The third pregnancy, in 1949, lasted nearly 14 weeks, and it was at this time that the patient first came under my care. When the second period was due there had been three small painless vaginal blood losses on consecutive days. She allowed a week to elapse before reporting to the clinic, and a pregnanediol estimation at the time revealed no evidence of progesterone deficiency. When the third period would have been due vaginal loss recommenced. She was admitted to hospital, and, in spite of complete bed rest, abortion occurred two weeks later. Evacuation of the uterus followed, and on examination under anaesthesia an indentation could be clearly felt in the position of the fundus. A finger passed through the open cervical canal identified a projection into the uterine cavity, the retained products of conception being found in the left horn.

The fourth pregnancy occurred in 1951, and the patient was seen after she had had seven weeks' amenorrhoea. She stated that one week previously a small red blood loss per vaginam had been noted, and this had been followed by a slight pinkish discharge every morning. Some days later, at the time when the second period was due, a further small fresh blood loss occurred, but with complete rest in bed and 2 gr. (0.13 g.) of phenobarbitone daily for seven days this symptom was not repeated. The time when the next period would have occurred was estimated and complete bed rest was again the regime adopted. Nothing untoward occurred. Progress appeared to be satisfactory until the 22nd week of pregnancy, when backache and a watery vaginal loss were followed by complete abortion. A male foetus was passed which was normal on inspection. Macroscopically the placenta showed no abnormality.

Eight months later a hysterogram was undertaken. One and a quarter hours after ¼ gr. (22 mg.) of "omnopon" had been administered hypodermically, an intrauterine injection of "viskiosol six" was given. The *x*-ray picture obtained is reproduced. The patient was naturally anxious about the outcome of any future pregnancies, and I advised that a further attempt might be made.

Radiograph showing uterus bicornis unicollis.

Three months later she began her fifth pregnancy. As had been previously arranged, she was admitted to hospital for complete rest in bed at the times when her periods would normally have been due. Progress was uneventful until the 26th week, when she was readmitted to hospital complaining of backache and watery discharge. These symptoms, however, were not apparent after admission, and three days later she returned home.

At 36 weeks the foetal position was left sacro-anterior. Maturity and the presentation of breech with extended legs were confirmed radiologically. No attempt at external cephalic version was made, and elective caesarean section was decided upon. The operation was performed three weeks later. Foetus and placenta were found to be occupying the left horn of the uterus and were delivered through a longitudinal incision in this horn, breech extraction of a female infant being achieved with no difficulty. The right horn of the uterus was hypertrophied and about the size of a 10-weeks pregnancy. A thick muscular projection extended from the indent in the fundus down to the level

of the internal os. The child appeared normal in all respects and weighed 5 lb. 12 oz. (2.6 kg.). Maternal and infant progress was uneventful.

COMMENT

In an attempt to assess what the chances of a successful conclusion to a fifth pregnancy would be I was influenced by the writings of Malpas (1938) and Eastman (1950). These authors estimated mathematically the "spontaneous cure rate"—that is, the chances of successful pregnancy—following any given number of successive abortions. Their calculations included both those abortions resulting from accidental or fortuitous factors and also those in which a recurrent cause was present. The figure arrived at by Malpas for the chance of successful pregnancy following four consecutive abortions was 6% and that of Eastman under 2%.

In the case here reported there was a most definite causative factor for the abortion, failure of approximation of the Müllerian ducts having led to the condition of uterus bicornis unicollis. The mathematical chances of a fifth pregnancy succeeding seemed very slight indeed. The decision to advise the patient to make a fifth attempt was taken because of the fact that the duration of each pregnancy had increased, abortion occurring at 8, 10, 14, and then 22 weeks. This suggested that each successive hypertrophy of the pregnant horn of the uterus made it more capable of containing the next pregnancy, and it was hoped that if this sequence were maintained a viable foetus might result. In this decision I was influenced, too, by the keenness of the patient herself to try again. Another alternative was to perform an abdominal metraplasty, but it was decided to await the outcome of this further attempt.

It is an established fact that when pregnancy occurs in one horn of a uterus the other undergoes hypertrophy and a decidual reaction occurs. Occasionally the non-pregnant horn continues to menstruate, and this bleeding at the time of a period from a pregnant bicornuate uterus is not necessarily indicative of threatening abortion. However, in this case the losses were followed by abortion on too many occasions for this symptom to be ignored, and thus rest over the time when the periods were due was regarded as important.

I am indebted to Mr. R. C. Thomas for permission to report this case, and to Mr. D. Lindsay and Mr. K. G. Seager for their helpful advice.

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Purpura following Manipulation of the Spine

The patient, a milk tester aged 42, is well known to me, as he has suffered for years from a contact eczema of the forearms. I have therefore had frequent occasion to inspect his skin, and before the episode described below he had not shown any purpuric manifestation.

On June 3, 1954, he was driving a motor-cycle combination with his head turned sideways to view a field of wheat, when he hit a small obstruction in the road. The jar was not excessive. Two hundred yards further on he tried to dismount, but found that he was unable to do so because of pain in his back. With considerable difficulty he got home and retired to bed. I saw him the next day and found him almost completely immobilized, with the now common syndrome, "the acute back."

On June 5 I asked an orthopaedic surgeon to see him on a domiciliary visit and he diagnosed, "joint lesions at L 3–4 joint on the left side, and the L 4–5 joint on the right side." These he mobilized by forward pressure on the left side of the third and on the right side of the fourth lumbar vertebra, with suitable positioning to lock the neighbouring joints. There was some relief of pain from this manœuvre.

On June 6 I was called to see him as a rash had appeared on both lower legs. The rash was a florid petechial one, extending from his toes up over his thighs. There was a large effusion into the right knee-joint and bilateral effusion into both ankles.

He was admitted to the skin ward of the Gloucester General Hospital for observation, where the rash and joint symptoms subsided over the next ten days.

Since that date I have seen another patient who was manipulated by an osteopath for a cervical lesion, and who exhibited two patches of purpura on the shoulder in the skin area supplied by nerves arising from the vertebral apertures manipulated. Blood, fragility, and clotting tests in this patient were all normal and his rash faded within two days.

The orthopaedic surgeon who manipulated the first patient told me that he had seen transitory eruptions following manipulation, but nothing of the magnitude of the case described. I make no suggestion about the mechanism of this phenomenon, but think it worth reporting as yet another cause of purpuric eruptions.

I thank Mr. J. Bourdillon for his orthopaedic care of this case, and Dr. R. E. Bowers for his advice and for admitting this case to his dermatological beds for observation.

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The Adrenal X-Zone in Kwashiorkor

Although information is available concerning the morphological changes in the human adrenal before and after birth, nothing is known of the function of the foetal X-zone of the cortex, which is most concerned in these changes. Anencephaly is the only condition definitely known to be associated with changes in the development and disappearance of this zone. Consequently the report by Gillman and Gillman (1951) that this zone persists in African infants dying of kwashiorkor is of great interest, since it would suggest a new approach to the physiology of this zone. As a first step in this direction it was necessary to confirm, if possible, the original observation.

The adrenals from seven cases of kwashiorkor in African children between the ages of 1 and 4 years were examined by methods used previously (Stoner, Whiteley, and Emery, 1953). They were compared with the adrenals from 19 other African children dying from a variety of causes, and with the adrenals from a larger series of English children (Stoner *et al.*, 1953). The behaviour of the foetal X-zone appeared to be the same in all three groups. No evidence of its persistence in the cases of kwashiorkor was found, and, so far as could be ascertained from these small groups, the rate of involution of the foetal X-zone after birth in the African adrenals was the same as in the English series and equally unaffected by systemic disease.

We have been prompted to report this negative observation since, with modern methods of treatment, fatal cases of kwashiorkor are becoming infrequent, and the original claim of Gillman and Gillman has now been reiterated in two reviews (Lanman, 1953; Baar, 1954).

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Reviews

PSYCHO-ANALYTICAL TECHNIQUE

The Technique of Psycho-analysis. By Edward Glover, M.D. (Pp. 404+x. 35s.) London: Baillière, Tindall and Cox. 1955.

Neither Freud nor any of the early pioneers in psycho-analysis ventured to write a full exposition of its technique. Perhaps they were acting on Bernard Shaw's cruel epigram, "He who can does; he who cannot teaches"; but more probably they were daunted by the endless ramifications of an enormously complex subject. The second generation of psycho-analysts were less restrained, and after the First World War several books appeared on technique. One recalls a very poor one in 1920 by Paul Bousfield, a fairly good one in 1922 by David Forsyth, and an excellent one in the same year by de Saussure. Then followed a series of six lectures by Edward Glover in 1928, which were published as a supplement to the *International Journal of Psycho-Analysis.* Since that time Dr. Glover has severed his connexion with other psycho-analysts. This has doubtless given him more independence, but has its own peculiar disadvantages.

The present book is made up of three parts. The first, longest, and most essential one consists of a greatly expanded version of the lectures just mentioned. The second is a record of a lengthy questionary Dr. Glover carried out in 1936–8 among British psycho-analysts. The main conclusion emerging from it is the extraordinary difficulty of formulating questions with sufficient precision to elicit comparable replies of value from different analysts. The third part is a reprint of three thoughtful essays that were published in the *International Journal* in 1931, 1937, and 1954 respectively.

The book is written in an easy, fluent, and vivid style, and is packed with the author's characteristic shrewd wisdom. Although ostensibly addressed to students, it can be read with profit by every practising psycho-analyst. So many detailed issues are raised in it that it would need a long technical essay to evaluate them properly, and this no doubt will happen elsewhere. In the meantime it can be hailed as a contribution of value to a difficult topic, and recommended to those who are directly concerned with it. It is well produced and has an excellent index.

ERNEST JONES.

EPSOM COLLEGE

Epsom College Register, 1855–1954. Edited by T. R. Thomson. (Pp. 620; illustrated. 31s. 6d.) Oxford: University Press for Old Epsomian Club. 1955.

Timed very accurately to anticipate the visit of Her Majesty, whose demonstration of her interest in the centenary of the College has gratified the whole of our profession, this *Epsom College Register,* as a labour of love on the part of Dr. T. R. Thomson and of the Old Epsomian Club, reflects the greatest credit on all concerned in its production, including the Oxford University Press. The introductory chapters, which are in fact a brief history of the school in its first hundred years of existence, should prove intriguing to the medical profession at large as well as to the considerable Epsomian section of it, and also to those of the general public who are education-minded. That the College has deserved well of the profession, so many of whose sons it has educated, especially by its provision of free places for those boys (and girls) left in straitened circumstances by early parental death and other causes, is a truism which there is no need to labour here. That it urgently needs financial help to carry out an essential programme of improved buildings and other amenities is equally true. The Council has for some months striven unceasingly to convince the medical profession of this, with a degree of success not as yet by any means commensurate with its truth. The production of this admirable volume may help to persuade those who chance to read it that the enterprise and vision of the Council really do deserve generous support. Of the *Register* itself it can be reported that it is well worthy to take rank among the best of the similar products emanating in recent years from public schools of similar standing. It is a splendid monument to the patriotism and piety of the Old Epsomian Club.

HENRY ROBINSON.

MODERN TRENDS IN OPHTHALMOLOGY

Modern Trends in Ophthalmology. Third series. Edited by Arnold Sorsby. (Pp. 346+xiv; illustrated. 65s.) London: Butterworth and Co., Ltd. 1955.

The purpose of a book such as this is to enable its reader to keep in touch not only with recently consolidated gains in knowledge but also with current trends in thought and experiments in technique through which the advances of the future may accrue. This volume, the third of its series, follows the general lines of its predecessors. Its 28 chapters divided into six sections cover such a diversity of subject-matter as to make a general appraisal difficult; the value attached to each section will vary with the interests, experience, and familiarity with the literature of each individual reader, but each section is not without interest, and the general balance is good. Those surgically inclined will welcome the chapters on corneal and retinal operations and on surgical technicalities, and another giving a clear exposition of the management of vertical squint. In the diagnostic and clinical fields are excellent and well-illustrated articles on, among other subjects, slit-lamp fundus microscopy, binocular ophthalmoscopy, and tonography; while particular recognition may be accorded to chapters on the nature of malformations and on the criteria of genetic affections, and to the section on social ophthalmology dealing with the problems of the blind and visually handicapped. Current views in relation to ocular pharmacology, collagen diseases, allergy, virus diseases, and the fitting of contact lenses are among other subjects discussed.

Some of the sections are so short and of such little apparent value or interest as to make the reviewer wish that they had been omitted to allow of the "selected bibliographies" having been made less selective; for example, in one chapter in which 36 or so authors are quoted in the text, only 12 references are appended. It is also perhaps unfortunate that in certain directions, particularly in an article on retrolental fibroplasia, and even allowing for the inevitable time-lag between writing and publication, the book's titular claim to modernity can hardly be upheld. Nevertheless this volume, excellently produced and well illustrated and indexed, will go a long way in helping to keep the ophthalmologist abreast of the times and in touch with the modern trends of his specialty.

A. J. B. GOLDSMITH.

RECENT ADVANCES IN TREATMENT

Modern Treatment Yearbook, 1955. Edited by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S. With 36 contributors. (Pp. 344+viii; illustrated. 25s.) London: For *Medical Press* by Baillière, Tindall and Cox, Ltd. 1955.

The Modern Treatment Yearbook, which comes of age in this twenty-first publication, is designed to keep the practitioner informed on the practical application of the latest research in medicine, using the latter term in its widest sense. Though the emphasis is on therapeutics, the yearbook includes more than a bare description of recent advances in treatment, for it recognizes that it is impossible to describe treatment adequately without defining the condition to be treated, which often involves some discussion on aetiology and diagnosis. It thus provides what is essentially an annual refresher course in medicine given by 36 physicians and surgeons, mostly chosen from those working in London or its environs. A great diversity of subjects is covered

in these 36 well-chosen articles, including, for example, the new insulins, Bornholm disease, blood-vessel grafting, temporal arteritis, growing pains, and prolonged labour. Though the book is a small one comprising only 344 pages, and though it is packed full of concise information, it is nevertheless eminently readable, even by an exhausted practitioner at the end of a long day. Instead of the tabulated instruction so popular in many current American therapeutic works of reference, each contribution in this book consists of a well-written short essay summarizing in excellent English, in simple terms, and with much wisdom the present state of our knowledge on a large number of subjects of current interest in which advances have recently been made.

This is a very good book indeed, and it was a most encouraging and unusual experience for the reviewer to find that there was nothing in it he could not understand.

D. M. DUNLOP.

GALEN

Galen of Pergamon. By George Sarton. (Pp. 112; illustrated. $2.50.) Lawrence, Kansas: University of Kansas Press. 1954.

English literature of the history of medicine is poor in reliable works on Galen and has very few translations of his writings. This is a serious deficiency. Hippocrates is at best a shadowy figure who may well have written nothing, and every member of the so-called "Hippocratic" collection is of disputable date and authorship. Most of them come from a world lit by a misty half-light of scholarship. But Galen is a real and very human figure, one of a world and circle familiar to philosophical historians. To them Galen's use of the experimental method is as well known as Harvey's, perhaps better. Moreover, it was the translation into Latin of Galen's works, and specially of his anatomical works, that set medicine on its modern scientific path, signposted by observation and experiment. Hitherto the only full account of Galen in English was in a scattered series of pleasantly readable papers by the late Dr. Joseph Walsh which are, unfortunately, not easily accessible. Thus Dr. Sarton in this handy little volume opens to English readers what is almost a new chapter in the study of ancient medicine.

Galen, as Dr. Sarton tells us, was a Greek of Asia Minor who studied at many centres in the East Mediterranean—then under complete Roman control. He spent several years at Alexandria. His writings are the chief source of our knowledge of the great medical school there. His most active and creative years were spent at Rome, where he was physician to Marcus Aurelius (Emperor, 161–180) and tutor to his son Commodus (Emperor, 180–192). He must have been very familiar with the Latin tongue, but his writings are all in Greek, the scientific lingua franca of his time. Of all this Sarton gives a concise and excellent account, wisely treating lightly the differences between the overwritten ancient "medical sects," the tedious and unclear exposition of which has repelled many readers of medical history. Sarton's booklet provides also good summaries of Galen's various activities, as anatomist and physiologist, as clinician, and as philosopher, with sections on his character, style, bibliography, and translation. Altogether a useful and well-timed little book.

CHARLES SINGER.

GYNAECOLOGY

Gynecology: Diseases and Minor Surgery. Compiled and edited by Robert J. Lowrie, M.A., M.D., F.A.C.S. Foreword by Claude E. Heaton, M.D. (Pp. 852+xix; 775 illustrations, 19 in colour. £8 2s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This work on gynaecology, the first of two volumes, is described as representing the culmination of many years of effort of 79 contributors from 30 medical schools and other institutions in the United States, Canada, and Great Britain.

The book, which is generously illustrated, covers the subject of gynaecology with considerable thoroughness, even including matters which seem more appropriate to undergraduate teaching. To remind graduate readers that the cervix is also called the "neck of the womb" seems unnecessary, as are two illustrations showing how a digital examination of the pelvic organs is carried out. Also, a number of opinions are expressed which will not be accepted in this country. For example, in the chapter on infertility there is the statement that "donor insemination is a needed and rewarding medical service"; even in America this statement is probably no longer acceptable now that an American judge in Chicago has ruled that, "except where donor and recipient are married to each other, artificial insemination is illegal and constitutes adultery on the part of the mother . . . and the children fathered by anyone but the mother's husband are illegitimate" (*British Medical Journal*, 1954, **2**, 1555). On a lighter level, it must be pointed out that the use of gin, 1–2 oz., for dysmenorrhoea is not "so highly regarded by the English School." There are some surprises, too; for example, a section describing in considerable detail the "Kenny" treatment in acute poliomyelitis. The claim is made in the foreword that due consideration has been given "to the role of the psyche" in gynaecological disorders, yet there is no separate chapter about this extremely important subject.

This book contains much wisdom: nevertheless its form and cost will not commend themselves to many in this country.

C. S. RUSSELL.

CRANIAL HYPEROSTOSIS

Hyperostosis Cranii. By Sherwood Moore, M.D. (Pp. 226+x; illustrated. 75s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955.

The syndrome of obesity, facial hirsuties, and frontal hyperostosis described by Morgagni and re-described by at least three other writers has been known to physicians for nearly two centuries. Dr. Moore has collected practically all the available information on this condition, to which he has added studies of his own.

He subdivides the syndrome into five types and elaborates the whole affair into something which, in the reviewer's opinion, is more complex than the facts justify. It is also suggested that frontal hyperostosis causes headache, fatigue, muscular weakness, nervousness, depression, diplopia, epileptiform seizures, impairment of memory, and other alarming symptoms. These features may have occurred in patients with frontal hyperostosis, but the evidence that they are caused by it is exceedingly uncertain. As regards the aetiology, the author's own words are: "The theory is advanced that hyperostosis and its syndrome are the manifestation of an endogenous intoxication traceable to aberrance in some unknown phase of the function of reproduction." It will be news to most doctors that cranial hyperostosis has social, economic, and palaeopathological aspects.

Although Dr. Moore's book does not throw any new light on Morgagni's syndrome, it must remain a valuable source book for those wishing to explore the subject; the bibliography runs to 315 titles.

A. M. COOKE.

Doctor to the Islands, by Tom and Lydia Davis, is an account of a young doctor, born and brought up on the Cook Islands, who returns from New Zealand to his old home as medical officer. Tom Davis is a self-confident and critical young man. He credits his predecessors with little knowledge and the administration of the Islands with a lack of interest in local welfare which is hard to believe. None the less the problems facing a doctor on the Cook Islands and on others in Polynesia, and the various methods adopted to try to solve them, make interesting reading, as do "Dr. Tom's" excursions into politics on behalf of the islanders. Medicine is not the only topic in the book, however, for Tom Davis took back to Rarotonga with him a New Zealand girl he had married and she has included her account of social life and conditions there. As husband and wife have written alternate chapters in the book the result is rather disjointed. For those who like sailing yarns the last few chapters give a lively story of a Pacific crossing in a small yacht at the worst time of the year. *Doctor to the Islands*, which is published by Michael Joseph, costs 15s.

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DEFENCE AGAINST ATOM BOMBS

On August 6, 1945, soon after 8 a.m., an American Superfortress bomber released an atomic bomb over the centre of the Japanese city of Hiroshima. More than 4 square miles (10 square km.) of the city were destroyed. The city centre was dominated by a number of reinforced concrete buildings owned by banks, department stores, and other commercial enterprises, while outside the centre lay a densely packed zone of small wooden workshops and lightly constructed dwellings. The destruction was due partly to blast and partly to fire, which took firm hold of the city about an hour after the attack and burned unchecked for days.[1] The population of Hiroshima was something under 300,000—or about the size of Coventry, though more straggling.[2] The population was considerably swollen at the time of the bombing by war workers and military establishments. It is believed that an alert had been sounded before the bomb was dropped but had been "relaxed." The number killed will never be precisely known; it is often estimated at 70,000–80,000, with about an equivalent number of injured. However, the Hiroshima city authorities placed the final toll of immediate and delayed deaths as 210,000 to 240,000.[3] The civil defence services, if they attempted to function at all, were overwhelmed by a disaster the scale of which was completely unforeseen. A photograph in a book published in 1953 by a committee of the National Research Council of Japan conveys more forcibly than any words the plight of the survivors. It shows[4] a group of more or less seriously injured people the day after the disaster, lying in the open, without shelter or shade, without food or water, without hope or comfort. Yet five miles distant was relatively undamaged terrain from beyond which might have come mobile medical and rescue teams and supplies—had they existed to meet a disaster on this scale.

Doubtless the efficiency of atomic weapons has been greatly increased since 1945, and estimates of the destructive power of the hydrogen bomb in particular are too well known to need recapitulation. However, it is at least uncertain if the most powerful weapons would be used in any new war. Smaller, though locally more highly destructive, atomic weapons have recently been developed, such as guided missiles, and projectiles that can be fired from an 11-in. (30-mm.) gun.[5] While it may be true that a small number of hydrogen bombs released over selected areas in Britain might paralyse defence and rescue work, this is unlikely unless an attack with smaller weapons were to be successfully developed. The lessons of Hiroshima and Nagasaki are therefore still relevant to our own civil defence, and they point to the need for an efficient civil defence service. Neglect to provide one cannot be excused on the ground that it might be rendered useless by a hydrogen bomb attack.

An important investigation on atomic bomb injuries in relation to the type of protection has recently been reported by two American workers,[6] who analysed the case histories of 5,136 persons injured at Hiroshima and interviewed 1,207 uninjured persons who had been exposed to the bombs. All these survivors reported that they had been within a radius of 13,120 ft. (2½ miles, or 4 km.) from the ground-centre of the explosion. Excluded from the analysis were a small number of uninjured persons within this distance, who were in tunnels or in air-raid shelters. Of the injured, more than half had mechanical injuries—lacerations and contusions—but remarkably enough no fractures were encountered. A. A. Liebow, S. Warren, and E. de Coursey[7] had earlier reported that, among the survivors of Hiroshima seen two months after the bombing, only 4.5% had fractures. They attributed this low figure to the fact that only those who were able to move escaped the flames. Some time elapsed—perhaps one hour—between the explosion and the spread of the fires. Burns afflicted 45% of the injured. All except three of these were due to flash and not to fire; most were confined to the extremities and were of second or third degree. Radiation effects were suffered by 34%; they were usually moderate, as might be expected in a group of patients who had survived several weeks to months after exposure. The absence of blast injuries was another unexpected finding. Those near enough to be thus injured must have been killed in this or some other way.

Unexpected, too, and with an important bearing on our own problems of civil defence, were the results of the analyses in relation to the class of protection.

[1] *Medical Aspects of Atomic Warfare*, 1948, War Office Publication, London.
[2] *Report of the British Mission to Japan* (*Effects of Atomic Bombs on Hiroshima and Nagasaki*), 1946, H.M.S.O., London.
[3] Kusano, N. (editor), *Atomic Bomb Injuries*, 1953, Tokyo.
[4] —— ibid., 1953, p. 22, Tokyo.
[5] Hunter, C. G., and Wedd, G. D., *Med. ill.* (*Lond.*), 1954, **8**, 754.
[6] Reynolds, M. L., and Lynch, F. Y., *Publ. Hlth Rep.* (*Wash.*), 1955, **70**, 26.
[7] Liebow, A. A., *et al.*, *Amer. J. Path.*, 1949, **25**, 853.

Of those people who were indoors or in heavy buildings at the time of the explosion 80–88% suffered mechanical injuries, as against 28% of those in the open. Moreover, the most severe mechanical injuries were in the people who were indoors or shielded out of doors. Doubtless the percentage of people remaining alive to tell of their experience was greater indoors than out, but those who were preserved indoors suffered injury from flying glass and debris, falling walls, and the like. The investigation clearly shows that severe mechanical injuries in each distance zone increased with increasing protection, and were incurred in one-half to two-thirds of the injured persons who were indoors in buildings of either light or heavy construction.

What are the lessons to be learnt from this survey? Clearly an investigation of the effects on survivors of an atomic explosion cannot give a true picture of the effects on the whole exposed population. Nevertheless, such an investigation can yield information of the utmost value for the planning of civil defence and rescue. Thus, if the interpretation of the low incidence of fractures in survivors is correct, probably a great many lives could be saved if people immobilized by injuries were removed to safety before the widespread fires get under way—about one hour after the explosions at Hiroshima and Nagasaki. In a western city, with a much lower proportion and density of timber construction, this interval might well be increased. The analysis of the injuries in relation to the type of protection affords, perhaps, the most unexpected finding; it seems clear that satisfactory protection can be given only by a structure built or adapted for this purpose, in which the risk of flying glass, plaster, or other debris is reduced to a minimum. Finally, there is the lesson of the flash burns, which injured about 45% of the survivors. Of all the atomic bomb hazards, that from heat flash is most easily avoided. Indeed, the thinnest layer of light-coloured fabric is sufficient to protect against it. Moreover, the moment that elapses between the light flash and the heat flash may be sufficient to enable those caught in the open to protect themselves from the latter. Evidently instruction in civil defence should be directed to the general public as well as to defence service personnel.

BANNING OF HEROIN

The quantity of heroin (diacetylmorphine) that the Home Office has authorized to be manufactured in the U.K. this year is 150 kg. Some of this may be exported, though none has yet been. In 1954 the amount manufactured was 198 kg., and of this the authorized quantity exported was 27 kg. The amount medically prescribed was perhaps something like 100 kg., since some might have been put into stock and some used for the manufacture of nalorphine. The number of doses to which this weight is equivalent would seem to be at least several million in a year. The drug is therefore commonly prescribed in Britain; and, since its universally known dangers of causing addiction would allow its prescription only after particularly careful thought, those doctors who claim that for some cases it has no satisfactory substitute would find many of their colleagues in agreement with them. Moreover, they cannot be accused of taking unnecessary risks with such a drug, for the number of addicts in this country is trifling. About forty are known to the authorities, and the strict control over supplies of the drug makes it most improbable that the true total can be much greater. The decision to ban its use altogether may therefore have been taken a little hastily, especially since a possible alternative exists which could be tried—namely, a ban on the export of the drug.

Repeating the Government's decision to prohibit the manufacture and export of heroin after December 31 next "except for small quantities for purely scientific purposes," Lord Mancroft[1] said that the ban was made in order to give effect to a resolution adopted by the Economic and Social Council of the United Nations, that the advice of the appropriate statutory bodies was taken, and that adequate supplies of a perfectly good substitute were available. In taking this step the British Government is falling into line with the great majority of the United Nations members—many of which have never had trouble with addiction to heroin—including Canada, Australia, New Zealand, and the U.S.A., and indeed only France, Belgium, and Italy have not yet agreed to a ban on manufacture or import. Those countries where the drug is prohibited are apparently satisfied with the consequences of this, several of them after some years' experience. Nor did opinion in Britain seem to be much different until fairly recently, and the monograph on heroin was omitted from the *British Pharmacopoeia* in 1953. The *National Formulary* contains no preparation of heroin; the introductory notes in the present edition[2] state that "its use could with advantage be reduced and reserved for parenteral administration." When the view was advanced in these columns two years ago[3] that in order to help to free the world from its thousands of heroin addicts the advantages of prohibiting its manufacture in

[1] *House of Lords Hansard*, Vol. 192, No. 48, Col. 595 (April 27).
[2] *National Formulary*, 1955, British Medical Association and Pharmaceutical Society of Great Britain.
[3] *British Medical Journal*, 1953, **2**, 196.
[4] Ibid., 1953, **2**, 338.
[5] Fifth Report of Expert Committee on Drugs Liable to Produce Addiction, *Wld Hlth Org. techn. Rep. Ser.*, No. 95, 1955.

Britain outweighed the disadvantages, Dr. A. H. Douthwaite's disagreement with that opinion[4] was left unsupported. But since then opinion has hardened, no doubt in part because clinical experience with the newer synthetic analgesics has increasingly shown that they do not meet the needs of some cases, and that heroin alone can do so. Incidentally, addiction to pethidine, according to the World Health Organization, is now reaching alarming proportions.[5] The B.M.A. considered the matter last year in response to a request from the World Medical Association, and the Council agreed that the medical profession should not be deprived of the use of this drug. As Dr. R. Hale-White points out elsewhere (p. 1277), this is a sufficient refutation of the opinion expressed in the House of Lords by Lords Mancroft and Haden-Guest that the whole medical profession is behind this Order. Further opposition to it is evident in motions sent in by B.M.A. Divisions (published in the *Supplement* this week at p. 242) for debate at the Annual Representative Meeting in June. Opinion seems on the contrary to favour the continued prescribing of the drug. All this, combined with the fact that the drug is widely prescribed with relatively little ill effect, suggests that alternative means should be sought for preventing the abuse of heroin. Surely the Government might well try authorizing production for home use only and place a ban on exports.

DENTAL CARIES

In 1947 a group of research workers from the United States and Canada met at the University of Michigan[6] to discuss the mechanism of dental caries. Last year the World Health Organization sponsored a seminar during which the aetiology of dental caries was discussed. From 1945 to 1951 the Royal Swedish Medical Board[7–9] carried out far-reaching experiments into the cause of dental caries. All agree that the prime factor in the cause of dental caries is the concentration of acid in the mouth and the length of time it is present on the tooth surface. Acids are produced by the fermentation of carbohydrate foods. Most of the food is swallowed; much that remains on the tooth surfaces is quickly washed away by saliva, and some of the acid produced by fermentation is efficiently neutralized. But small areas on the tooth surface are sheltered from the forces of mastication and the stream of saliva, and food stagnates there. When fermentable particles of food lodge in these areas several times a day and, owing to their sticky nature, remain there for some time, these particular sites on the tooth surface become carious. The total quantity of fermentable carbohydrates consumed is therefore subsidiary to the frequency with which they are taken, their time relationship with other foods, and their physical consistence.

Experiments and observations show that dental caries is increased by impaired salivary flow, by a lowered buffer capacity of the saliva, or by an increase in the frequency of taking sticky fermentable carbohydrate foods into the mouth; it is decreased by the avoidance of such foods, reducing the frequency with which they are eaten, alteration of the consistence of the food so that it does not stick to the teeth, or by introducing specific enzyme inhibitors into the mouth. Although tooth structure has some influence on whether caries occurs or not, the decisive factors are usually conditions on the tooth surface.

The findings of the Medical Research Council's recently published report[10] on "The Effect of Sugar Supplements on Dental Caries in Children" cause no surprise. Extra sugar was given with their meals to test groups of children in three areas in England, but the control groups were not without considerable amounts of sugar and other fermentable carbohydrates, for both groups took their full sweet, sugar, and jam ration in two areas and breakfast cereal and bread *ad lib.* in all three. Both test and control groups, therefore, had sugar and wheat flour products, and both showed much the same amount of dental caries. Such alteration in percentage of sugar in a meal has been shown in animal experiments[11 12] to have little effect on dental caries, and in the Swedish experiments sugar was shown to have the least effect when taken with other foods. The number of children taking part in the M.R.C. experiments was small, and the authors state on page 30 of the report, referring to the largest of the three studies: "The small number exposed to risk prevents any definite conclusions being drawn. . . ." It is surprising to find, however, that the extensive Swedish experiments have not been mentioned.

NEW TESTS OF HEARING

The eight years which have followed the publication in 1947 of the report on hearing-aids and audiometers[1] by the Electro-Acoustics Committee of the Medical Research Council have witnessed notable advances in the functional investigation of hearing. For example, the methods of speech audiometry prescribed by the committee have enabled otologists to measure accurately not only the essential handicap of the deaf subject—namely, his inability to understand the spoken voice—but also the extent to which this handicap can be corrected by means of hearing-aids and otherwise. In addition to these improvements in the measurement of hearing loss, the qualitative analysis of it has also been the subject of important developments. Thus in 1948 M. R. Dix, C. S. Hallpike, and J. D. Hood,[2] of the Medical Research Council's Otological Research Unit, demonstrated for

[6] *Dental Caries* (ed. Kenneth A. Easlick), 1948, London.
[7] Lundqvist, C., *Oral Sugar Clearance, Odontol. Rev.*, 1952, **3**, Suppl. 1.
[8] The Vipeholm Dental Caries Study, *Acta odont. scand.*, 1954, **11**, 232.
[9] *British Medical Journal*, August 8, 1953, p. 331.
[10] *Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), No. 288, 1955. H.M.S.O., 4s.
[11] Mitchell, D. F., *et al.*, *J. dent. Res.*, 1951, **30**, 778.
[12] Wakeman, E. J., *et al.*, ibid., 1948, **27**, 489.

[1] *Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), No. 261, Hearing Aids and Audiometers, 1947, H.M.S.O.
[2] Dix, M. R., *et al.*, *Proc. roy. Soc. Med.*, 1948, **41**, 516.
[3] Hood, J. D., *Acta oto-laryng.* (*Stockh.*), Suppl. XCII, 1950.
[4] Rüedi, L., *Schweiz. med. Wschr.*, 1954, **84**, 1411.
[5] Tschirren, B., ibid., 1954, **84**, 1414.

the first time that the phenomenon of loudness recruitment, first described by Fowler, of New York, and considered by him to be a general characteristic of "nerve" deafness due to lesions of any of the cochlear nervous elements, was in fact pathognomonic of lesions of the hair cells of Corti's organ. By contrast, in cases of deafness due to lesions of the cochlear nerve fibres, loudness recruitment was characteristically absent or incomplete. As a result of this work, now widely confirmed, tests for loudness recruitment have become valuable in making the important clinical distinction between end-organ deafness and nerve-fibre deafness.

Results of comparable clinical value have also accrued from the work of J. D. Hood[3] on cochlear fatigue and adaptation. Hood carried out a number of exact studies of the deafening effect on the normal human ear of prolonged exposure to pure tones, and he was able to show that this deafness underwent an abrupt increase when the stimulus intensity exceeded a certain critical level. Hood was also the first to give a clear account of the phenomenon of cochlear adaptation, a particularly elusive variety of deafness which occurs during and immediately after the application of a sustained sound stimulus. Its rapid disappearance on removal of the stimulus makes the phenomenon exceedingly difficult to investigate, and its demonstration was possible only by means of an ingenious test carried out during the application of the stimulus.

The clinical importance of cochlear adaptation and of the methods since developed for its measurement lies in the fact that it undergoes a striking increase in cases of deafness due to disease of the neural elements of the cochlear apparatus, in particular the hair cells of Corti's organ. Thus it comes about that in cases of deafness of obscure origin clinical investigation of cochlear adaptation provides valuable evidence of whether or not the cochlear end-organs are affected.

As might be expected, these delicate methods of investigation of the functional state of the cochlear end-organs are beginning to prove of exceptional value in the investigation of the early stages of its derangement by disease or injury, and a notable example has recently been provided by the work of L. Rüedi[4] and others,[5] of Zurich. These workers have used them for investigating the effect of vitamin A in protecting the cochlear end-organs from injury by prolonged pure-tone stimulation. In Rüedi's experiments a group of normal subjects were exposed to prolonged pure-tone stimuli of high intensity, and the critical intensity level was determined. Repetition of the tests after a period of high vitamin-A intake revealed a marked increase in the critical level, indicating an increase in the resistance to injury of Corti's organ. Functional changes of this kind could not be revealed by any of the usual tests of cochlear function, such, for instance, as pure-tone audiometry carried out according to the usual technique. The successful use by Rüedi and his colleagues of these new methods of investigation of cochlear function, therefore, gives grounds for the hope that otologists elsewhere will find in them an equally valuable instrument for the investigation of the early stages of cochlear disease or injury.

HEALTH SERVICES IN NORTHERN IRELAND

The report[1] of a committee set up by the Government of Northern Ireland "to advise on criticisms and suggestions made by members of both Houses of the Northern Ireland Parliament about the operation of the health services" is summarized in this week's *Supplement*. Two out of three members of the committee, the chairman of which was Mr. H. G. Tanner, have been closely associated with the development of hospital and health services in Great Britain. Such criticisms of the health service as have been voiced in the Northern Ireland Parliament seem mainly to have been directed to the system itself—not to any laxity or maladministration which may have occurred, but to the possibility of such occurrence should the good sense and restraint which have hitherto characterized the service be diminished. The main complaint is that parliamentary control over health services is ineffective, and that too much power is in the hands of nominated bodies or corporations which cannot readily be called to parliamentary or governmental account.

In Northern Ireland there has been a devolution of responsibility which does not obtain in Great Britain. The Ministry of Health and Local Government is not empowered itself to provide health services, but only to promote or secure their provision and co-ordination, which it does mainly through a Hospitals Authority and a General Health Services Board. The Ministry has thus a less positive role in administration than the Ministry of Health in England, and parliamentary critics have complained of the Hospitals Authority in particular as autocratic in dealing with hospital management committees and hospital staffs, and as stultifying local initiative. The Tanner Committee scarcely subscribes to these criticisms. It finds that the Hospitals Authority has shown itself energetic, that it has many achievements to its credit, and that there is no foundation for any charge of irresponsibility or extravagance. Nevertheless, it agrees that its relationship with the Ministry is anomalous, and that the position both of the Authority and the General Health Services Board in regard to the Ministry should be that of agent to principal. The system which has been found successful in Great Britain should be adopted in Northern Ireland.

A large number of detailed recommendations are made by the committee, but so far as general medical services are concerned their effect would be to alter the position very slightly. One recommendation concerning consultants is that their contracts should be reviewed at regular intervals; another is that distinction awards should no longer be made by the Authority but preferably by a single committee having jurisdiction over the whole of the United Kingdom, to which Northern Ireland advisers should be attached. But in general the report presents a picture of the health services of Northern Ireland—where there has been greater freedom to incur capital expenditure than in England and Wales and Scotland—as in a state of vigorous and continuous growth.

[1] *Report of the Committee on the Health Services in Northern Ireland*, Cmd. 334, H.M.S.O., Belfast.

INBORN DEFECTS OF THE RENAL TUBULE

Fanconi attributed the syndrome popularly associated with his name to a genetically determined defect of the renal tubule. It is only recently, however, that attempts have been made to relate this syndrome to a number of hitherto distinct metabolic lesions, whose underlying cause appears to be a failure in function of the proximal tubule.[1-4] This part of the kidneys is concerned in the reabsorption of water, glucose, amino-acids, phosphate, bicarbonate, calcium, and possibly potassium, so that a wide variety of single or multiple biochemical abnormalities may be predicted as likely to follow disordered function here. The best-known single defect is renal glycosuria, but renal diabetes insipidus also occurs occasionally, and is characterized by extreme polyuria which is insensitive to posterior pituitary extract. Amino-aciduria occurs in hepato-lenticular degeneration (Wilson's disease) and in congenital cystinuria. It has been suggested that cirrhosis of the liver in the former results from the drain of amino-acids, though it is possible that both the hepatic and the renal lesions are secondary to the accumulation of copper. Faulty reabsorption of phosphates leads to vitamin-D-resistant rickets, while hyperchloraemic acidosis (Albright's syndrome) may be the result of a failure to reabsorb bicarbonate, with a compensatory increase in chloride reabsorption. Idiopathic hypercalcuria has also been reported, though hypopotassaemia has not been recognized as a single defect. Theoretically any combination of defects might be expected, but so far only a few are well defined. Glycosuric rickets appears to be a specific entity, though in many cases amino-aciduria has not been looked for. Glycosuria has been noted in some patients with Wilson's disease. The triple resorptive defect of glucose, phosphate, and amino-acids occurs in the classical Fanconi syndrome, and it is interesting that in some of these patients also the metabolism of water, bicarbonate, and potassium may be disordered; cirrhosis of the liver is a well-recognized complication. Cystinosis, in which cystine is deposited in the tissues, is usually considered to be a variant of the Fanconi syndrome, and may be accompanied by glycosuria and hypophosphataemia.

Although these diseases were originally found in children, a number of cases have been reported in adults[3 5 6]; many of these were originally termed Milkman's syndrome because of the pseudo-fractures and osteomalacia. They are presumably milder forms of the inherited defect, though it is conceivable that acquired lesions or some other inborn error of metabolism may be responsible. It is important to realize that these conditions do not give rise to renal failure in the accepted clinical sense except occasionally as a terminal complication, and death usually results from dehydration, acidosis, or intercurrent infection. The limited necropsy material from cases of the Fanconi syndrome has invariably shown degenerative changes in the proximal convoluted tubule. The absence of phosphatase from this part of the kidney led to the view that deficient phosphorylation is responsible for the faulty reabsorption.[5 6] However, E. M. Darmady has recently shown, by painstaking micro-dissection of individual nephrons from two cases, that the proximal tubules are abnormally short and are joined to the glomerulus by a thin "swan-like" neck.[7] Further work on other examples of the group, using both histochemical and histological techniques, will be awaited with much interest. There is no doubt that the new classification will help to clarify many defects which are at present obscure. Prognosis has already been improved by the introduction of measures designed to counteract the metabolic disturbances. Massive doses of vitamin D, alkalinizing regimes, and the replacement of water and potassium are all important, and there is some experimental evidence that methyltestosterone may have a beneficial effect on renal tubular function.[8]

[1] McCune, D. J., *et al.*, *Amer. J. dis. Child.*, 1943, **65**, 81.
[2] Jackson, W. P. U., and Linder, G. C., *Quart. J. Med.*, 1953, **22**, 133.
[3] Myerson, R. M., and Pastor, B. H., *Amer. J. med. Sci.*, 1954, **228**, 378.
[4] Singer, M., *J. Bone Jt Surg.*, 1954, **36-B**, 633.
[5] Stowers, J. M., and Dent, C. E., *Quart. J. Med.*, 1947, **16**, 275.
[6] Cooke, W. T., *et al.*, *Arch. intern. Med.*, 1947, **80**, 147.
[7] Clay., R. D., *et al.*, *J. Path. Bact.*, 1953, **65**, 551.
[8] Anderson, I. A., *et al.*, *Quart. J. Med.*, 1952, **21**, 33.

NEW LOOK IN PHYSICAL MEDICINE

Taunts of therapeutic empiricism and false pathological conceptions based on therapy have in the past often been directed at the specialty of physical medicine. Some degree of empiricism is probably inevitable in a specialty which has grown up slowly over the course of centuries, so that many of its methods are surrounded by an aura of traditional sanctity, and Dr. W. S. Tegner,[1] in his Samuel Hyde Memorial Lecture, scrutinizes ruthlessly the scientific basis of most of the treatments which are still being used in orthodox departments of physical medicine. He refutes absolutely the conception of a specialist in physical medicine being concerned only with therapy: in point of fact he must be a skilful diagnostician in view of the wide range of disorders from which his patients may be suffering. In addition, he is in the best position to undertake the long-term planning and management of chronic disorders of the locomotor system, such as rheumatoid arthritis. Tegner admits the strong suggestive influence of many physical treatments, and proceeds systematically to destroy some popularly held misconceptions on massage, electrical currents, ionization therapies, ultra-violet light, and various forms of heat treatment. He favourably reviews the recent experiments which have put short-wave therapy on a sound scientific basis and, conversely, have failed to show that microwave therapy and ultrasonics have advantages compensating for their expense and danger. He criticizes the use of such meaningless jargon as "tonic effects" and "removal of waste products and metabolites," and also the multiple names by which a single mode of treatment may be known—for

[1] *Proc. roy. Soc. Med.*, 1954, **47**, 389.
[2] *Ann. phys. Med.*, 1954, **2**, 75–85.

example, constant current, direct current, or galvanism, all of which mean the same thing. Finally, he commends the newly developed electrodiagnostic techniques as examples of the recent scientific trends in physical medicine and as excellent research weapons.

At the annual meeting of the British Association of Physical Medicine last year Drs. A. C. Boyle, A. T. Richardson, and R. Doll contributed to a symposium on "The Scientific Approach."[2] They discussed in more general terms the imperative necessity of applying a statistical scrutiny to all new forms of therapy before they are accepted, and of reviewing as soon as possible all the classical methods still in use. In each case three questions had to be answered: "Is this treatment of value?" "Of how great a value?" "And with what type of patient?" None of these speakers eschewed the use of "placebo" remedies, provided that the physician was perfectly clear about the nature of his prescription and chose an inexpensive and harmless method of achieving the desired result. Another point made by all the contributors to this discussion was the importance of understanding the natural history of the disease being treated, and of realizing the potentiality it had for spontaneous remissions. Doll, speaking from the statistician's point of view, once again emphasized the dangers of "general impressions" in therapeutics, and the pitfalls in using theoretical considerations in developing a new approach rather than the essential test of "Does it work?" Specialists in physical medicine have often been challenged to subject their techniques to scientific validation, and it is a healthy sign that they should now be critically examining the methods by which the specialty can achieve its objects of restoring the patient to health and of making a useful contribution to medical research.

GENETICS OF CONGENITAL HEART DISEASE

Large-scale studies of the families of children with congenital heart disease have been published only in the last few years. Before then selected individual families had been reported. For example, G. C. Walker and L. B. Ellis[1] recorded the case of a father and four of his eight children all with signs of patent ductus arteriosus, and M. Campbell[2] recorded signs of auricular septal defect in three generations. In neither of these families was there full post-mortem or operative confirmation of the nature of the lesion. In addition, genetic factors are known to play a part in the causation of certain syndromes with which congenital heart disease may be associated. For example, situs inversus, partial or complete, is in some cases at least due to recessive genes,[3,4] and cardiac malformations in addition to dextrocardia are commonly present in this condition. Congenital heart lesions are also often found in association with arachnodactyly, which is usually due to a dominant gene.

In 1953 T. McKeown and his colleagues[5] gave an account of the family histories of 437 children with congenital heart disease who had been born in Birmingham between 1940 and 1949. They found a small but definite increase in the incidence of congenital heart disease among the brothers and sisters of these index cases. Their estimate of the general incidence at birth was 3.2 per thousand, but among the 352 sibs born after their index cases six were affected, five of whom were also index cases in the series. It was noteworthy that in the two fraternities with two affected children in whom the precise lesion was known the pair of affected sibs had the same lesion, in one pair transposition of the great vessels, in the other a ventricular septal defect. Non-cardiac malformations did not occur with undue frequency in sibs. In only two instances were the parents first cousins, and in both the malformation was dextrocardia with transposition of the viscera. This year P. E. Polanyi and M. Campbell[6] have reported on the families of 386 children attending Guy's Hospital. Their findings are similar. Of 635 sibs whose condition was known, 9 had congenital heart disease, and 6 of the 265 born after the index case were affected. Here, too, there was a tendency for the affected sibs within a fraternity to have the same or similar lesions. While Polanyi and Campbell thought that the incidence they found of non-cardiac malformations among the sibs (2%) was unduly high, it is doubtful if this is really so. In only three instances were the parents first cousins, and in one of these the child was one of the few patients with transposition of viscera.

Specific types of congenital heart disease are evidently apt to be concentrated in certain fraternities, but the risk of subsequent children having congenital heart disease is not high and of the order of 1 in 50. If simple genetic factors are at work they must have a low penetrance, and this is supported by the finding that usually only one of a pair of monozygous twins is affected.

It is desirable for genetic analysis to break down congenital heart disease into specific types. This will become possible as more operations are performed on cases of congenital heart disease, making exact diagnosis possible. R. C. Anderson,[7] of Minneapolis, Minnesota, has made just such a study of 105 families in which the index case was proved at operation to have patent ductus arteriosus without other cardiac defects (four other children were excluded because of a known maternal history in pregnancy of rubella). Of 145 sibs born after the index case, two had patent ductus arteriosus and one of these also had coarctation. Since the general incidence of patent ductus arteriosus is almost certainly less than 1 in 5,000, Anderson's data show a familial concentration. None of the sibs in this series had any type of cardiac or non-cardiac malformation. All of the four probably monozygous twins of index cases were unaffected.

There is no convincing evidence that maternal age or birth order or season of birth affects the incidence of congenital heart disease. Sex, however, plays a part; coarctation of the aorta occurs mostly in males and patent ductus arteriosus mostly in females. Polanyi and Campbell[6] show that aortic stenosis, Fallot's tetralogy, and transposition of the great vessels also occur predominantly in males.

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[1] Walker, G. C., and Ellis, L. B., *Proc. New Engl. Heart Ass., 1940–1*, 1940, 26.
[2] Campbell, M., *Quart. J. Med. (N.S.)*, 1949, **18**, 379.
[3] Cockayne, E. A., ibid., 1938, **7**, 479.
[4] Torgersen, J., *Amer. J. hum. Genet.*, 1950, **2**, 361.
[5] McKeown, T., *et al.*, *Brit. Heart J.*, 1953, **15**, 273.
[6] Polanyi, P. E., and Campbell, M., *Ann. hum. Genet.*, 1955, **19**, 209.
[7] Anderson, R. C., *Pediatrics*, 1954, **14**, 143.

EMERGENCIES IN GENERAL PRACTICE

TREATMENT OF SEVERE ASTHMA

BY

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The development of the first really severe attack of asthma is an alarming event for the patient, for the patient's friends, and, at times, for the doctor. Usually there has been some previous evidence of an asthmatic tendency which may have amounted to little more than discomfort. Then an attack of tightness in the chest lasts longer than usual, increases in severity, and the patient's efforts become concentrated simply in trying to breathe out the air which overfills his lungs. Any attempts his relatives or friends make to help are of little avail and their distress at standing by and watching his gasping respirations only too often adds to the patient's alarm. It is in this atmosphere that the doctor finds himself. Successful treatment depends to a great extent on the tacit assumption that the attack can and will be treated successfully. It is rare for an asthmatic attack to be fatal, unless it occurs in elderly patients, or is complicated by other conditions, such as spontaneous pneumothorax, or unless wrongly treated by respiratory sedatives.

Much depends on the way in which the situation is handled. The doctor must be prepared to give up time to the patient's treatment, and time spent in initial treatment is time saved in the long run. The patient will usually have found the position which gives greatest relief, either sitting forward in bed or sitting up in a chair.

Antispasmodic Treatment

Treatment of the bronchospasm should be begun at once. It is rare that adrenaline is unsuccessful, provided it is given correctly, and it is important to give it with care when first used. Once the patient appreciates its use he will look forward with confidence to its benefits during subsequent attacks; if it is used inadequately it may need much persuasion and perseverance on the next occasion to overcome his prejudice against it.

A dose of 5 minims (0.3 ml.) of adrenaline, 1 in 1,000, is given hypodermically. If this dose does not give relief after 10 minutes, adrenaline should be injected at the rate of 1 minim (0.06 ml.) a minute, keeping the needle *in situ*, until the spasm is relieved. In this way large doses of adrenaline can be given without ill effects.

In those cases in which adrenaline is ineffective, aminophylline can be given. It is best administered by intravenous injection, the contents of one ampoule containing 0.25 g. in 10 ml. of water being injected slowly. This can be repeated after four hours, and if necessary the dose can be doubled provided the total of 20 ml. is given slowly. Intravenous treatment may usefully be supplemented by giving the aminophylline in a rectal suppository. This is a convenient way of maintaining some antispasmodic action over a prolonged period and is particularly useful for administration at night.

Antihistamine drugs are usually of little help in relieving severe asthmatic attacks.

Sedatives

During the acute stage sedative treatment is usually inadvisable. As the attack passes off, small doses of sedative can be given to calm the patient and to help ward off another attack. Phenobarbitone in ½-gr. (32-mg.) doses is usually effective. Opium derivatives and large doses of barbiturates are contraindicated. The patient's life may depend on his respiratory efforts, and depression of the respiratory centre, particularly by the use of morphine, may prove fatal.

Oxygen

If there is marked cyanosis, oxygen will often help the patient. It should be given with a B.L.B. mask or "polymask." The administration of oxygen, however, may distress the patient more than benefit him, as the application of anything over the mouth or nose may increase the sense of suffocation, and the very suggestion of oxygen may be associated in the patient's mind with the terminal stages of severe illness.

A.C.T.H. and Cortisone

A.C.T.H. and cortisone are on occasions of definite use in treating asthma, but, with our present knowledge, they should be used with caution. A.C.T.H. and cortisone are given in doses of 100 g. in divided doses six-hourly during the first 24 hours and continued, with reduced dosage if possible, for three or four days; cortisone can be given by mouth. There is no doubt that in many instances this treatment will give definite relief. If, however, the treatment has to be repeated, its results, using the same dose, may be disappointing and an increased amount will be required to produce the same effect. Large doses and more continued treatment are not without danger to the patient. At the present time it is probably advisable to withhold these remedies, giving them only when there is urgent need. They are usually called for in treating elderly patients with emphysema who are in great distress and in danger of developing cardiac failure, and also in cases in which the acute attack is prolonged and is developing into status asthmaticus.

Status Asthmaticus

If the attack becomes prolonged, with no remissions, and extends over a period of several days and nights, the condition then is indeed a difficult one to treat. It is advisable whenever possible to remove the patient from home surroundings, preferably into a hospital. The atmosphere of a hospital ward, with efficient nursing and the knowledge that there is always medical help at hand if required, will do much to quieten the patient. Continuous treatment with aminophylline can be carried out if required by slow intravenous drip, using 0.5–1.5 g. of aminophylline in a litre. At this stage the patient is often suffering from some degree of dehydration, since the continued breathlessness has made drinking and eating difficult or almost impossible. By giving aminophylline intravenously, the necessary fluid can be supplied, and it may be useful to use 5% glucose–saline as the vehicle for the drug. The patient should also be encouraged to take sips of water by mouth. When cyanosis is marked, an oxygen tent may be necessary. Cortisone or A.C.T.H. may be required and should be given if other treatments have been tried and failed, or, as already indicated, should be given to patients with severe emphysema or cardiac failure.

Treatment after the Attack

As soon as the attack has been controlled, it becomes necessary to take steps to prevent another attack developing. A small dose of sedative such as phenobarbitone, ½ gr. (32 mg.) two or three times during the day will often quieten the patient. The first evidence of recurrence of wheezing or tightness in the chest should be treated immediately. An

injection of adrenaline, 3 to 5 minims (0.2 to 0.3 ml.) should be given at once. The earlier this is done, the more likely it is to ward off a fresh attack. If it is not possible for the doctor to give the injection immediately, it is often advisable for suitable patients to be taught how to give the injection to themselves. When this is not feasible, ephedrine, ½ gr. (32 mg.), or isoprenaline, 20 mg., can be taken in tablet form, isoprenaline tablets being dissolved slowly under the tongue. Atomizers may be used to give adrenaline or isoprenaline by inhalation. Many of the proprietary preparations for the treatment of asthma contain one or other of these drugs together with phenobarbitone. Aminophylline suppositories given in the early part of the night may help to prevent an attack in the early hours of the morning. Some patients find antihistamine preparations beneficial, if taken as soon as the first symptoms of spasm are noticed. Expectorant mixtures containing potassium iodide and ammonium carbonate relieve those patients who have difficulty in coughing up sputum after an attack and are of particular use for patients who have chronic bronchitis complicated by asthma.

It is now recognized that one of the most successful treatments in controlling the incidence of attacks and in controlling an attack in its early stage is breathing exercises. If the patient conscientiously practises those exercises which encourage proper diaphragmatic breathing and full expiration, he will be able to reduce the number of attacks and also can often abort an attack. The breathing exercises can be combined with postural exercises when there is evidence of localized chronic infection in the bronchial tree.

Prevention of Pulmonary Infection

Care should be taken to detect pneumonic lesions during the period after an asthmatic attack, particularly in those patients who suffer from chronic bronchitis. During an asthmatic attack, bronchi or bronchioles may become plugged with thick mucous secretion, with resultant segments of collapsed lung beyond. Usually re-expansion takes place, but at times the collapsed portion of the lung becomes infected and prompt treatment with antibiotics is indicated if this complication is suspected.

Next article on Emergencies in General Practice.—"Post-partum Maternal Collapse," by Miss Josephine Barnes.

Refresher Course Book.—Copies of the second volume of collected articles from the Refresher Course for General Practitioners published in the *Journal* are still available at 25s. (postage 1s.) each. The volume contains 60 articles, all of which were revised by their authors for publication in the book. The first volume is now sold out and out of print. Copies of the second volume may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

PRACTICAL ADVICE ON HEARING-AIDS

In a lecture at the Institute of Laryngology and Otology, London University, on April 29 Mr. J. CHALMERS BALLANTYNE, assistant director of the audiology unit of the Royal National Throat, Nose, and Ear Hospital, discussed the indications for advising a hearing-aid, the choice of a suitable instrument, and the way to get the best results from it.

The ability of a deaf person to hear with an aid, said Mr. Ballantyne, was determined very largely by the type, as well as the degree, of his deafness, and it was essential to have a clear understanding of the differences between the two broad types of deafness—perceptive (or "nerve") deafness and conductive (or "middle-ear") deafness. The hearing apparatus had two parts, a perceiving apparatus and a conducting apparatus. The perceiving apparatus consisted of the end-organ of hearing itself—that is, the organ of Corti—and the acoustic nerve and its central connexions. The conducting apparatus consisted of the external auditory canal, the middle ear, and the Eustachian tube. It also included the fluids of the inner ear. Its function was to conduct sound-waves from their source to the end-organ, amplifying them to some extent as it did so. Perceptive deafness resulted from any lesion in the perceiving apparatus, while conductive deafness was due to lesions in the conducting apparatus. The two types of deafness could nearly always be distinguished from one another by a careful history, a thorough clinical examination, and a single tuning-fork.

Indications for the Use of Hearing-aids

There were very few deaf people who could not derive some benefit from using an aid, continued Mr. Ballantyne, and it was much better to start using one too early than too late. When deafness was purely conductive in nature, as in early cases of otosclerosis and in suppurative disease of the middle ear, the perceiving apparatus was normal. In theory, all that was required to allow such a patient to hear normally was to amplify sounds to such a degree that they would reach the normal perceiving apparatus at a normal degree of loudness. In practice also, the necessary amplification could usually be provided by an electrical hearing-aid.

When deafness was purely perceptive, as in the deafness following meningitis or the deafness of old age, the problem was much more complex. Amplified sounds reached the *abnormal* perceiving apparatus with the same degree of loudness as in the normal ear, sometimes even louder. But they were distorted sounds, often uncomfortable and sometimes painful. And it was characteristic of perceptive deafness that, beyond a certain point, the ability to understand speech became reduced and not enhanced by further amplification. On the other hand, many patients suffering from perceptive deafness could derive real benefit from an electrical aid.

Construction of Electrical Aids

Since the second world war the design and construction of electrical hearing-aids had improved enormously. Aids consisted of three parts: a microphone, an amplifier, and a receiver. The microphone converted sound energy into electrical impulses; the amplifier amplified the sounds; and the receiver converted the electrical impulses back into sound energy.

The Amplifier.—Most electrical aids used a system of thermionic valves, the power required by this system being provided by two batteries. A low-tension battery warmed the filaments in the valves, and a high-tension battery provided the power for the amplification. Many commercial firms are now substituting the so-called "transistor" valve for the thermionic valve.

The Receiver.—There were three different types of receiver: the insert receiver, the flat receiver, and the bone-conduction receiver. The insert receiver fitted into the ear itself and was by far the most commonly prescribed. It should be made to measure for each individual user. It could be used even in the presence of active middle-ear discharge, provided that the ear was cleaned regularly by simple aural toilet and the insert kept free from discharge. An external otitis might result in a few cases, when the use of an insert must be discontinued, at least temporarily. The flat receiver was worn with a headband. It was large, uncomfortable, and now rarely prescribed. Leakage of sound was almost invariable, with consequent "howling." The bone-conductor receiver also caused considerable discomfort by the presence of a headband, but it might be indicated in some cases of aural discharge with external otitis. In a very limited number of cases of conductive deafness, not exceeding 2% of all hearing-aid users, it might give a very good performance. One commercial firm now produced a bone-conductor receiver carried on a spectacle frame.

Choice of an Aid

The choice, continued Mr. Ballantyne, lay between the Government aid and a commercial one. The "Medresco" aid (the name being derived from Medical Research Council) was a duo-pack aid—that is, the batteries were carried separately from the microphone and amplifier. Its designers intended to produce an efficient aid, at the lowest possible cost, and of value to the greatest possible number of deaf persons. In these objects they had largely succeeded. The size of the batteries was perhaps the greatest single disadvantage of the Government aid, for they were large and undoubtedly cumbersome. On the other hand, they lasted much longer than smaller batteries and were cheaper to produce. And much smaller batteries were available, at the patient's own expense, which could be used with the Government aid (*low tension:* Ever Ready B 119, Siemens S 119, Drydex D.H. 519; *high tension:* Ever Ready D 18, Siemens S 18, Drydex D.L. 14). Improvements to the Medresco aid were gradually being made, and a smaller model should be available before very long. The aid itself was issued free to any deaf person considered by an otologist to be likely to benefit from its use. It was obtainable at any hearing-aid distribution centre, where repairs were also available. Batteries could be replaced at any hospital.

Commercial aids were nearly all of the mono-pack type—that is, the batteries were included with the microphone and amplifier. They were lighter in weight, less conspicuous, and much more comfortable to wear. In some, but by no means in all, said Mr. Ballantyne, the performance also was better than that of the Medresco. Their great disadvantage was, of course, the cost, which varied roughly from £15 to £35 for thermionic-valve aids, and was approximately £20 more for "transistor" aids. Maintenance and repairs added considerably to the burden. The choice of a commercial aid should be made only after trying several under all the normal conditions of the patient's life. The aid should be tried not only at home but in the office, church, theatre, and the like.

The National Institute for the Deaf had an approved list of manufacturers and was always ready to offer advice on this matter. Test reports were also made on commercial aids by members of the Medical and Scientific Committee of the Institute.

It was claimed for the newer transistor aids that maintenance costs were considerably reduced, since only one battery was needed, with a working life of up to 200 hours. But their ability to withstand hard, constant wear remained to be proved.

It was often advisable to consult an agent who stocked a variety of makes before making a final decision.

The Wearing of an Aid

Many deaf persons were opposed to the idea of wearing an aid. It advertised their disability, so they thought. Little did many of them realize how much more obvious it was when they refused to wear one. In women the aid could easily be worn without any sign of its presence. The receiver could be hidden by an appropriate hair-style, and the lead likewise made invisible. In children the various parts of the aid could be distributed by means of a home-made harness, details of which were obtainable from the Deaf Children's Society. All children, the speaker continued, should be provided with the smaller mono-pack type of aid, but this ideal was not yet attainable.

A person with only a mild or moderate degree of deafness might need an aid only for hearing at a distance, as in a church or theatre. Many otosclerotics heard better in noisy surroundings than in quiet rooms—the phenomenon of "paracusis." In the noisy surroundings of certain occupations they therefore found an aid unnecessary and uncomfortable. Most other users, depending on professional or social necessity, should wear their aids all day.

When there was only a slight difference in the degree of deafness in the two ears the aid should be worn in the better ear. This meant less amplification and therefore less distortion, which in turn meant less battery consumption and less expense. The deaf person with an aid should sit as near as possible to the speaker. The further away he sat, the greater was the amplification needed and the more uncomfortable the background noise became. In a theatre, concert hall, or conference room the deaf person should sit as near as possible to the centre of the hall or table. With practice, an aid could be used quite satisfactorily with a telephone, and some commercial firms made a special adapter for this purpose.

Rehabilitation

It was impossible to over-emphasize the importance of careful instruction in the use of a hearing-aid. It was not enough to hand it "over the counter," so to speak, and expect the deafened person to hear immediately. Many an aid had been relegated to the bottom drawer within a month or so through failure to realize this.

Nor did the doctor's duty end there, for other "aids" to hearing might be needed to obtain full benefit, and every possible clue to the meaning of speech must be utilized. Auditory training taught the patient to distinguish, or discriminate, the many complex sounds of speech. And visual training, better known as lip-reading, enabled him to fill in the many visual clues to the pattern of speech.

Finally, said Mr. Ballantyne, many patients asked whether the continued use of a hearing-aid would cause deterioration in their hearing. Most patients who used aids suffered from a progressive deafness, but there was no evidence whatsoever that the use of an aid would, *per se*, affect the hearing adversely.

THE QUEEN AT EPSOM COLLEGE

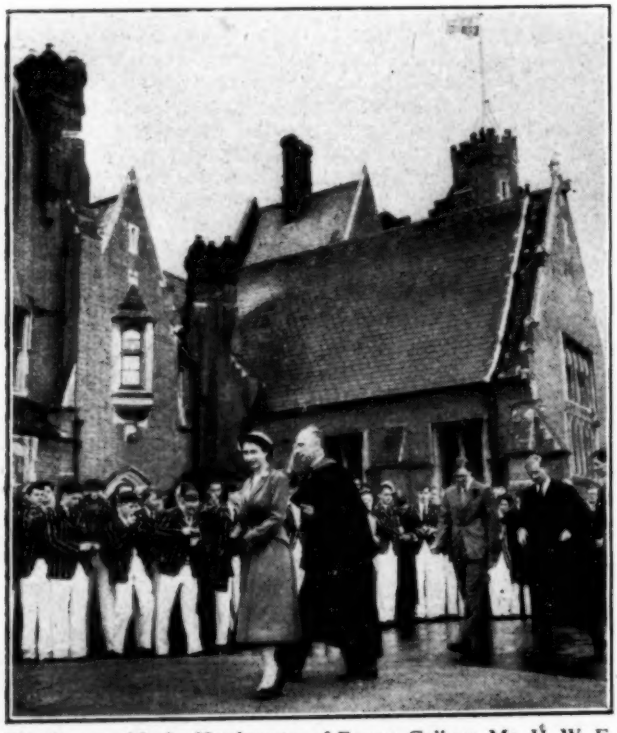
The Queen and the Duke of Edinburgh visited Epsom College on Friday afternoon, May 13, and inspected the buildings and grounds. The visit took place almost exactly 100 years after Her Majesty's great-great-grandfather, the Prince Consort, opened the College on June 15, 1855. The skies were uncertain, but the picturesque red brick buildings of the College standing in 90 acres of Epsom Downs framed a very happy occasion. The Queen, who is the College patron, was welcomed on arrived by General Sir Robert Haining, Lord Lieutenant of the County of Surrey, who presented the High Sheriff (Colonel the Hon. Guy Cubitt) and the Mayor of Epsom (Councillor Langston), and the Mayor in turn made other local presentations. Then, with the Royal Standard flying above the school buildings, the Queen inspected a guard of honour formed of the combined cadet corps. Lord Webb-Johnson, President of Epsom College, presented Dr. Henry Robinson (treasurer), Mr. R. W. Raven (chairman of the College council), Air Marshal Sir Lawrence Pendred (president of the Old Epsomian Club), and Mr. H. W. F. Franklin (headmaster). Accompanied by the last-named, Her Majesty and the Duke of Edinburgh made a leisurely and informal tour of the school, visiting the boys' rooms, the chemistry, physics, and biology laboratories, watching the pupils at work at the benches—Epsom was one of the first public schools to install such laboratories in the early 'seventies—the natural history museum, the art school, the carpenters' shop, and the assembly hall, where members of the dramatic society were giving a performance of *Twelfth Night*, with a very spirited Malvolio. The royal party next visited the chapel, where a surpliced choir of some 40 boys sang an anthem. The sporting and athletic side of the College was also in evidence—on the cricket pitch, and in the fives court (near which the remains of an early Bronze Age man were discovered a few years ago), the gymnasium, and the rifle range. A pause was made at the sanatorium, a building of modern design, with 58 beds, operating theatre, and

x-ray apparatus; here the royal party were received by the medical officer and the resident matron. The whole tour lasted an hour and a half, after which tea was taken in the headmaster's house in the company of the ladies of the College and the prefects. Before leaving, the Queen and the Duke planted trees in commemoration of the College centenary.

Epsom's Links with Medicine

Epsom College was founded 100 years ago by John Propert, who was a member of council of the then Provincial Medical and Surgical Association, afterwards the British Medical Association, and one of the first presidents of the Metropolitan Counties Branch. It was originally known as the Royal Medical Benevolent College, though it was never intended that it should be exclusively for doctors' sons or for boys intending to be doctors. About one in three Epsomians enter the medical profession, and the centenary register shows this to have been roughly the proportion throughout its history. But the College has always had a special claim upon the charities of the medical profession. Out of its complement of 350 boarders and 150 day boys, 62 at present are Foundation scholars, all sons of members of the medical profession in necessitous circumstances, most of them orphans; those who need it have everything paid; others are helped according to their needs. Further, in addition to 25 leaving scholarships available for boys studying medicine, scholarships are awarded to Epsomians every year by nine London teaching hospitals. Like other public schools, Epsom College has found it difficult to modernize its buildings and equipment out of its ordinary financial resources, and a centenary appeal, of which readers of this journal have already been reminded, has been made for not less than £150,000 in order that the school may "embark with confidence on a second hundred years of vigorous life and useful service to the community." Such an appeal cannot need many words of commendation to members of the medical profession.

The Queen in the Biology Laboratory.



The Queen with the Headmaster of Epsom College, Mr. H. W. F. Franklin. (Photos by Bippa.)

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

ANNUAL CONGRESS: LONDON, APRIL 28-30

This year's meeting of the Ophthalmological Society of the United Kingdom, held under the presidency of Mr. O. GAYER MORGAN at the Royal Society of Medicine, was most successful. From a wide variety of subjects discussed, four have been chosen for summary here. First, the clinical aspects of retinal vein thrombosis, the subject of Mr. Gayer Morgan's presidential address; secondly, the use of "diamox" (acetazoleamide) in glaucoma; and, lastly, two examples of modern ophthalmic techniques—the intraocular injection of air, and the use of radioactive isotopes in tumour diagnosis.

Retinal Vein Thrombosis

The seriousness of thrombosis of the retinal veins, said Mr. GAYER MORGAN, lay in the fact that it produced permanent visual disability in such a large proportion of cases. In the eye the close proximity of the arterioles and veins in the optic nerve and at their crossings made it possible for sclerosis of retinal arterioles to involve the adjacent walls of the veins. While in the kidney, the heart, and the brain the main factor leading to thrombosis was slowing of the blood stream in the arteries, in the eye the veins were affected more as a result of involvement of the common adventitia than because of stagnation, in spite of there being often concomitant arterial disease.

Treatment in the past had resolved itself into a review of the general health and the use of vasodilators. But now, said the president, it seemed that anticoagulants had a useful part to play in the treatment. They might prevent extension of the clotting or promote recanalization. There was also the possibility of using them prophylactically in cases of threatened venous thrombosis. One of the essentials for the rational use of anticoagulants was the recognition of the prethrombotic state. Patients with two good eyes often delayed attending until complete thrombosis had occurred, but those who had lost the sight of one eye from a previous thrombotic episode came up immediately they noticed their symptoms and so treatment could be started in the prethrombotic period. The ultimate outlook varied. There

might be absorption of the blood and reappearance of normal vision and an apparently normal vein; or a narrow and sheathed venous vessel might persist with many new collaterals, but even in this latter case there was no loss of field, so the blood supply to the retina must be adequate.

Mr. Gayer Morgan then described four cases which he had himself observed carefully over a period of time. From these he concluded that if anticoagulants were to be really useful they should be administered when a retinal vein was found to be dilated, when extravasation of blood was minimal, and while visual acuity was still good.

Action of Diamox in Glaucoma

Mr. E. S. PERKINS opened the symposium by discussing the clinical aspects. Diamox had a quick action, he said, and might reduce the ocular tension in all types of glaucoma. After a few days' use it might become less effective, but combined with miotics there was an additive effect. In a series of many varieties of glaucoma he had found the tension was reduced and kept so in 48% of cases; it was reduced but failed to remain within normal limits in a further 38%; while in 14% it was unaffected. Diamox was used initially in doses of 500 mg. at once and 250 mg. six-hourly, and later reduced to 250 mg. twice or thrice daily. Its chief use was as a pre-operative drug, particularly in acute congestive glaucoma, but it was disappointing as a therapeutic measure in patients with long-standing congestive attacks. The side-effects consisted of diuresis, nausea, vomiting, and paraesthesiae in the limbs. Mr. Perkins also discussed the possible modes of action of diamox. The drug was known to inhibit the enzyme carbonic anhydrase, and he described experiments showing that this enzyme is present in iris and ciliary tissue.

Dr. J. GLOSTER described experiments designed to measure the extent and rate of change in intraocular pressure induced by diamox when given intravenously to rabbits in a dose of 50 mg. per kg. of body weight. Intraocular pressure was continuously measured manometrically, and blood-pressure readings were also taken. In general, the intraocular pressure was reduced by 3 to 5 cm. of water in 15 minutes in the rabbit and the effect began two to three minutes after the administration of the drug.

Dr. M. LANGHAM, from his observations on the entrance of fluorescein into the eye, believed that the rate of flow of aqueous was reduced after the injection of diamox. There was no evidence that the drug produced an increase in permeability of the blood–aqueous barrier, as shown by measuring the accumulation of ascorbic acid and fluorescein in the eye before and after its use, nor was there any evidence to suggest that it acted by decreasing the resistance to drainage. Studies on the *p*H of aqueous humour and its ionic content did not answer the question of whether diamox acted specifically on the formation of aqueous humour by neutralizing carbonic anhydrase in the eye, or whether the results on intraocular pressure were of a secondary non-specific character.

In the discussion Professor G. P. SOURDILLE and Mr. A. PALIN gave some interesting clinical experiences with diamox in glaucoma. Dr. DOROTHY CAMPBELL showed how the plasma sodium and the degree of diuresis varied with the changes in intraocular pressure after the use of diamox in patients with glaucoma, and Sir STEWART DUKE-ELDER summarized the present standing of the drug.

Use of Air in Ophthalmology

Mr. H. B. STALLARD said that the intraocular injection of air had been used in ophthalmology therapeutically for the treatment of tuberculous iritis, diagnostically as an aid to the location of intraocular foreign bodies and intra-orbital neoplasms, but chiefly to help in the anatomical replacement following operations. After cataract extraction air was injected into the anterior chamber to re-form this and to keep the iris and vitreous face away from the wound; following cyclodialysis for glaucoma, air checked bleeding, re-formed the anterior chamber, and kept the fistulous tract open; after the operation for retinal detachment air in the vitreous restored the normal anatomical position of the retina; it was of value in the operation of keratoplasty to keep the bed of the transplant away from the iris and lens; and in the division of anterior synechiae air could be used to put the synechiae on the stretch and facilitate intraocular instrumentation. Air was compressible, continued Mr. Stallard; it produced a spring-like pressure, its site in the eye could be controlled by posture, and it was absorbed over a period of four to eight days. These were the properties which made it so useful in ophthalmology. The dangers attending its use, air embolism and the production of glaucoma, were almost negligible. Sterilization of the air was achieved by autoclaving a syringe with the plunger withdrawn.

Radioactive Isotopes

Mr. ANTHONY PALIN and Dr. R. C. TUDWAY read a paper on the use of radioactive isotopes in the diagnosis of intraocular tumours. The technique had practical importance because it was often difficult to distinguish clinically between malignant and non-malignant neoplasms in the eye. However, the excess take-up of such isotopes by most actively growing tumour tissue had now been amply verified. The authors used radioactive phosphorus (P^{32}) which with its short-range beta emissions appeared to give significant findings on the Geiger-counter. Adult patients were given 1 millicurie of radioactive phosphorus in water, sucked through a straw, and 24 hours later Geiger-counter readings were taken by a medical assistant or technician who had no knowledge of the site of the tumour. These readings were taken in the various meridians of the affected eye, and controls were taken from the symmetrical meridians in the fellow eye. The statistical error of the method was plus or minus 15%. In general (save in very small or very posterior tumours) the significant difference between the two eyes was taken as 40% or over. The cases of malignant tumour which the authors had studied showed a significant differential reading, and there was only one case, which had a low total, and therefore unsatisfactory, count, where the results of the method were misleading. In the discussion it was pointed out that the results did not depend on pigmentation of the tumour but rather on hyperactive cell metabolism; that most of Mr. Palin's cases were clinically suspect before the test was used; that, in the acute stage, uveitis might produce a misleading result; and that the method as at present developed was not of value in gliomata in young children.

Reports of Societies

RADIOACTIVE ISOTOPES

SYMPOSIUM AT ROYAL SOCIETY OF MEDICINE

[FROM A SPECIAL CORRESPONDENT]

Looking back over the past decade of clinical experience with artificial radioactive isotopes, one gets the impression that many people were apt at first to be too enthusiastic about the part this new tool would play in therapy and diagnosis. It was clear, however, from the tone of all the speakers at the symposium arranged by the Section of Medicine at the Royal Society of Medicine on April 26, that work with radioisotopes is now entering a period of more balanced assessment and comparison with other methods.

A B C of Radioisotope Therapy

The therapeutic uses of radioisotopes depend upon the fact that when the atoms of an unstable element disintegrate they emit radiations capable of destroying the tissues through which they pass. These radiations are of three kinds: (1) Electrons, or beta particles, which penetrate up to

about a millimetre of tissue; (2) gamma rays, which are electromagnetic radiations of rather shorter wavelength than *x* rays and which penetrate several centimetres of tissue; and (3) alpha particles, emitted only by the heavier elements and having a penetrating power much less than that of beta particles. Each unstable isotope emits radiations with a characteristic penetrating power and each has a characteristic rate of disintegration. The "half life" of different isotopes varies from a fraction of a second to millions of years.

A radioisotope is handled by the body in the same way as the naturally occurring stable isotope. Moreover, radioisotopes can be measured in minute amounts by means of their radiations. If, therefore, a substance normally present in the body is labelled by adding to it a negligible amount of the corresponding radioactive material, we can follow the way in which the substance moves about the body or is metabolized. This may be done either by measuring the radioactivity in serial samples of body fluids, or, as with some of the radioiodine tests of thyroid function, by measuring the gamma radiations with a detector outside the body. This is the basis of the increasing number of clinical tests in which a radioisotope is used.

Methods of Localizing the Dose

If a radioisotope with suitable properties can be brought into or near a tissue it may be possible to destroy that tissue without undue damage to near-by organs. In a sense, this new branch of radiotherapy can be regarded as an extension of the older technique of local irradiation by implanting radium or radon seeds. But, owing to the wide choice of radioisotopes now available, it has been possible to devise other more satisfactory methods for achieving a local effect.

Dr. E. E. POCHIN (U.C.H., London), opening the discussion, dealt in broad outline with the principles underlying these methods. The surface of the body might be irradiated by local application of a beta-ray emitter, he said, instancing the extensive use of P^{32} in surface applicators for the treatment of superficial lesions of the skin. A solution of radioactive material could be injected directly into the lumen of a hollow viscus or introduced inside a rubber bag. Both these methods had been used for irradiating superficial tumours in the mucosa of the bladder. Another way was to inject the radioactive material as a colloidal suspension into a solid tissue. In the colloidal state most of the injected material was retained at or near the injection site. Colloidal gold^{198}, for example, had been used in a variety of malignant tumours.

A more promising use of radiogold lay in the treatment of malignant effusions, continued Dr. Pochin. If colloidal radioactive gold were injected into the peritoneal cavity, it was rapidly deposited upon the peritoneal membrane. From this position malignant metastases were irradiated by beta radiations. However, since the beta rays of Au^{198} were of low penetrating power, the damage to the metastatic deposits was confined to a thin shell over their surface, unless they were very small. This might help to explain why radiogold appears to have no useful effect in some cases, while in others it led to marked improvement.

If small radioactive colloidal particles were injected intravenously they would accumulate in the reticulo-endothelial system and irradiate selectively those organs which contain a high proportion of R.E. cells. This principle had been tried in the treatment of the reticuloses and of a few primary tumours of the liver (using radioactive colloidal gold). If, however, large particles, 30 to 50 microns in diameter, were injected intravenously, they were arrested in the lung capillaries, whence they might irradiate the lungs selectively. If the injection could be made by cardiac catheter into one pulmonary artery, the irradiation could be localized in one lung. The first attempts to develop this method had been made with carbon particles coated with radioactive gold. But this had the disadvantage that distant organs might be damaged by the gamma rays of Au^{198}.

Metabolic Localization

Perhaps the most spectacular, and certainly the most successful, therapeutic use of radioisotopes, went on Dr. Pochin, was based on what might be called "metabolic localization." If the radioactive material was given internally in the form of a chemical substance which naturally accumulates within a particular organ or tissue it might be possible to achieve a high and uniformly distributed radiation dose without undue irradiation to the rest of the body. The two most promising examples of this were the use of radioiodine (I^{131}) in the treatment of thyroid disease and of P^{32} in the treatment of polycythaemia vera. The thyroid concentrated iodine to such an extent that the intensity of radiation delivered to the thyroid from a dose of I^{131} might be several hundred times as great as the radiation to the rest of the body. For this reason it was always possible to destroy selectively a normal or overactive thyroid gland by means of radioiodine. At present it would be fair to say that radioiodine provided a useful alternative to surgery and the antithyroid drugs in selected cases of Graves's disease and toxic nodular goitre. Radioiodine was simpler and less unpleasant to the patient than either of the former methods, and it entailed no immediate hazards. There was, however, still a possibility that carcinoma might arise in those parts of the thyroid which had been irradiated but not destroyed. No cases of cancer of the thyroid attributable to radioiodine had yet been reported among the many hundreds treated and followed for five years or longer. But most people agreed that, until more experience had accumulated, radioiodine should be used in the treatment of the non-malignant thyroid only if the patient was past middle age or if there was appreciable risk from other forms of treatment.

In malignant disease of the thyroid radioiodine was the treatment of choice if there were metastases which had the power to concentrate iodine. Generally, the tumours most likely to concentrate radioiodine were the most highly differentiated.

Concluding his remarks, Dr. Pochin stressed the great possibilities for the further development of radioisotope techniques. While it was probable, he said, that new methods would be introduced, whereby better local radiation effects could be obtained in tissues, of equal importance was the gradual improvement in methods of selecting patients. This was also one of the points stressed by the next speaker, Professor Smithers.

Experience at the Royal Marsden Hospital

Professor D. W. SMITHERS gave a brief survey of the results of work with radioisotopes over the past four years at the Royal Marsden Hospital (formerly the Royal Cancer). This survey included, among many other topics, the diagnostic use of I^{131} in thyroid disease, studies of the blood circulation by means of Na^{24}, measurement of red blood cell volume with red cells labelled by Cr^{51}; and the therapeutic uses of I^{131} in thyroid carcinoma, P^{32} in polycythaemia, and colloidal gold in malignant effusions.

With regard to the therapeutic applications of radioisotopes, said Professor Smithers, in some cases there was already enough experience to show that the new treatment had something useful to offer the patient for whom previously there was little else. This was certainly true of radioiodine in the treatment of iodine-concentrating metastases from a thyroid carcinoma. To a lesser extent it seemed true also of Au^{198} in the palliative treatment of malignant effusions, but it might be several years before it became possible to pick out with any confidence those patients most likely to derive benefit from this treatment. In other cases, as, for instance, the infiltration of prostatic tumours with Au^{198}, doubts about the wisdom of increasing tissue tensions in malignant disease even with radioactive materials had held back workers in Britain until the results of trials by others were available. Again, artificial radioisotopes had in a few cases been adopted because they had some slight practical advantage over the older methods. Such was the case with tantalum^{182} wire, which

appeared to be superior to radon seeds in the treatment of superficial tumours of the bladder, and with implants of gold[198] grains, which might supersede radon seeds in the treatment of some types of tumour.

Professor Smithers showed two films—one demonstrating the therapeutic uses of isotopes by surface, intracavitary, and interstitial application; the other the treatment of a young woman with malignant disease of the thyroid, a tracheotomy, and metastases in the neck nodes and lungs. This patient was treated by radioiodine. The tumours all regressed, and nearly six years after the treatment she was in normal health, with no clinical or radiological evidence of disease. Professor Smithers was careful to point out that this was an exceptional case.

Radioisotopes in the General Hospital

The last speaker, Mr. N. VEALL (Guy's Hospital), discussed the value of radioisotopes in diagnosis and research. He stressed the fact that radioisotope techniques were applicable in almost every branch of medical research, and quoted several examples to show how some of the methods developed for research had been adapted for routine clinical use. It was now possible for diagnostic tests to be carried out in the smaller hospitals, since the necessary equipment for most of the established procedures involved a capital expenditure of less than £200. When the volume of work justified such a course specialized equipment was available for carrying out particular tests on a mass scale. In some hospitals, for instance, hundreds of radioiodine tests of thyroid function were performed each year.

Another speaker asked whether every general hospital should be allowed to embark on work with radioisotopes, or whether it ought to be restricted to a few large centres. Mr. VEALL was rather of the opinion that the apparatus needed for many diagnostic tests was now so cheap and so simple to operate that any medical centre wishing to use it should be encouraged to do so. However, Professor SMITHERS pointed out that when isotopes were used for treatment adequate facilities must be available if only to ensure, among other things, proper precautions against radiation hazards by everyone concerned and for the disposal of radioactive wastes. He thought it would be uneconomical to have more than a limited number of radiotherapeutic centres throughout the country; and therapy, at least with internally administered isotopes, would tend to be confined to the larger medical centres.

LOCAL MEDICAL SOCIETIES

Manchester Medical Society

Some of the difficulties in diagnosing ankylosing spondylitis, and their bearing on treatment, were stressed by Dr. J. SHARP, lecturer in rheumatic diseases at Manchester, at a meeting of the Section of Medicine on March 23. In the majority of spondylitis patients referred to a special clinic for *x*-ray treatment, said Dr. Sharp, the disease conformed strictly to the generally recognized picture, and 70% of them were much improved by deep *x*-ray therapy. In the remainder, the disease had unusual features, and of these only 31%, a very significantly smaller proportion, derived similar benefit from treatment. There was evidence that the difference in the effects of treatment was due to inclusion in the "atypical" group of some patients with rheumatoid arthritis affecting the spine, of others with psoriatic arthropathy with spinal involvement, of a few with Reiter's disease, and of some who had developed a form of spondylitis following repeated and prolonged attacks of rheumatic fever, and that these conditions were usually unresponsive to *x*-ray therapy. Further, immobilization usually had an adverse effect in ankylosing spondylitis, while it was often helpful in these other conditions. About a third of the patients in the "atypical" group did not seem to fit into any of these categories, and Dr. Sharp suggested that other, as yet unrecognized, conditions might be represented.

Nova et Vetera

GLOUCESTERSHIRE ROYAL HOSPITAL

This year the Gloucestershire Royal Hospital celebrates the bicentenary of its foundation, and on May 3 the occasion was honoured by a visit of the Queen and the Duke of Edinburgh. A thanksgiving service was held on May 8 in Gloucester Cathedral.

In 1754 certain benevolent people in the city and county of Gloucester decided to form a charity to found and endow the Gloucester General Infirmary for "the cure of the sick and lame of any County or Nation, who are destitute of the means of support." The ample pecuniary return so quickly made to the appeal on the first formation of the charity in 1754 enabled the promoters of the scheme to act with promptitude. The conclusion being formed that the erection of a new building would be the most satisfactory course, land called the Talbot Ground near the South Gate was purchased, on which the present buildings now stand.

To prevent delay in offering to the poor the advantage of the charity, the Crown and Sceptre Inn, Westgate Street, was purchased for the sum of £300, fitted up as a temporary hospital, and opened for the immediate reception of patients on August 14, 1755. To mark this occasion an inauguration service was held in Gloucester Cathedral, followed by a dinner at the Bell Hotel, both being attended by most of the leading persons in the county and city.

On July 18, 1761, the new building, which had been erected at a cost of £6,200, was publicly opened after a service at the cathedral and a dinner at the King's Head Hotel, presided over by Sir Onesiphorus Paul. At that time the four principal wards in the new building were named "Beaufort," "Berkeley," "Benson," and "Talbot," and the total beddage was 116.

The Old Infirmary (the Crown and Sceptre Inn) was sold in 1765. In 1813 the Squirrell Inn and other property adjoining the Infirmary on the south side was purchased for £1,000, and in 1827 the south wing to accommodate 54 patients was erected at a cost of £4,745, thus increasing the number of beds to 170. In 1877 the hospital was established as a training school for nurses, and since that date many thousands of students have received their training and gained their certificates through the excellent teaching facilities provided.

In 1878 another institution in Gloucester, called the Gloucestershire Eye Institution, was closed and all the cases were transferred to the General Infirmary. The Infirmary thereupon, under an arrangement with the Eye Institution, created an ophthalmic department, and the hospital became known as the Gloucestershire General Infirmary and Eye Institution.

On June 23, 1909, on the occasion of the visit of H.M. King Edward VII to the Royal Agricultural Show held in Gloucester, it was made known in the reply to the address of the Gloucester Corporation that His Majesty had been graciously pleased to accede to the request of the hospital committee to use the prefix "Royal," in the name of the Institution, "in recognition of the admirable work done by those responsible for its management, and the devoted and successful efforts of its staff in the prevention and alleviation of human suffering," and thereafter it was called the Gloucestershire Royal Infirmary and Eye Institution.

In July, 1948, the hospital was taken over under the National Health Service Act, and the newly appointed group management committee decided that the other hospital in the city, known as the City General Hospital, previously administered by the local authority, should become part of the Royal Hospital, and the two are now one unit, known as the Gloucestershire Royal Hospital.

C. J. ADAMS,
House Governor.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Army Pathology

SIR,—In his interesting annotation on Army pathology (*Journal*, April 30, p. 1087) Major-General A. Sachs omits all mention of one of its most notable contributions to medicine—namely, the first clear account of the pathology of syphilitic aortitis. In 1875, Francis H. Welch, Assistant Professor of Pathology at Netley, gave a paper at the Royal Medical and Chirurgical Society entitled "On Aortic Aneurysm in the Army and the Conditions Associated with It." The paper was published in the *Medico-Chirurgical Transactions* in 1876.[1] Welch showed that aneurysm was due not to strain, as usually supposed, but to a diseased condition of the aortic wall which preceded dilatation. He gave an accurate account of the macroscopic and microscopic features of the aortic lesion, and distinguished it from atheroma. By reference to the medical history sheets of soldiers dying from aneurysm, he was able to show conclusively that a high proportion had been treated for syphilis, a fact difficult to prove in civilian cases before the advent of the Wassermann reaction.

It is evident that syphilitic aortitis had not escaped notice at Netley before Welch's time, for Myers, in his *Essay on Diseases of the Heart among Soldiers*,[2] mentions that Dr. Aitken had recognized aortitis in cases of aneurysm and had regarded it as syphilitic. Prior to this, a good deal of inquiry had been directed to the cause of aneurysm in soldiers, and the widely accepted explanation was that it arose from a hypertrophied heart ejecting blood with excessive force. The cause of this cardiac hypertrophy was supposed to be tight clothing and accoutrements, combined with strain, alcoholism, and other factors.

Though Welch's classical paper received inadequate recognition at the time, and his views were disputed, to-day it is generally accepted as the pioneer account of syphilitic aortitis. Both Allbutt and Osler so regarded it, and historians of cardiology such as Herrick, and Willius and Dry, have paid proper tribute to Welch's work. The centenary of Army pathology warrants some reference to it.—I am, etc.,

London, W.1. D. EVAN BEDFORD.

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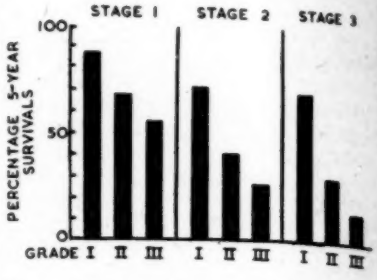
2 Myers, A. B. R., *Essay on Diseases of the Heart Among Soldiers*, 1870. London.

Classification of Breast Cancer

SIR,—Anyone who is concerned about the present unsatisfactory state of affairs in assessing the treatment of breast cancer will readily agree with Mr. Michael Harmer's plea (*Journal*, March 26, p. 790) for a standardized internationally accepted scheme of clinical staging. That such an anatomical yardstick is necessary in comparing the results of any form of treatment of malignant disease will be agreed by all. Unfortunately, however, in breast cancer the problem is not quite as simple as this.

For any system of staging to be of real value, accurate information regarding the involvement of regional nodes must be available. Clinical determination of axillary node involvement is incorrect in about 20% of cases with enlarged glands and 40% of cases with impalpable glands; and although routine histological examination of these glands gives a more accurate assessment even this may fail to reveal small metastases unless serial sections are cut.[1] In the majority of patients supraclavicular gland involvement is based entirely upon clinical examination, and the state of the internal mammary nodes is ignored. Thus any system of classification of breast cancer based entirely upon clinical staging can only be an approximate guide to prognosis.

An attempt to present a more accurate classification was made by grouping cases according to both clinical stage and histological grade.[2] The Manchester staging system and the method of grading introduced by Patey and Scarff[3] were used: the results are shown in the diagram.



It is evident that each stage contains representatives of three types of tumour, each bearing a different prognosis. Grade III cases are seen to account for many of the failures in Stage 1, and Grade I cases for the successes in the more advanced stages. It is postulated that the histological grade of malignancy provides a measure of the probable extent of the growth, those of low grade tending to remain localized to the primary site and those of high grade tending to metastasize early. This may compensate, to some extent, for the omissions and errors which may arise in the clinical assessment of glandular involvement.

We agree that an international method of staging breast cancer is urgently required, but we feel that to use a system of clinical staging alone in comparing the results of treatment would be to neglect the most significant denominator of all—namely, the inherent degree of malignancy of the cancer cells. Such a course, in our opinion, would only serve to increase the confusion that already exists.—We are, etc.,

H. J. G. BLOOM.
London, W.1. W. W. RICHARDSON.

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Anxiety Neurosis

SIR,—However much I lack the urge to effort for common welfare, I cannot let Dr. Ronald A. B. Rorie's article (*Journal*, April 30, p. 1062) pass in silence. I fear the silence, hence my attempt to combat it. As you see from the article, Dr. Rorie occupies an important position in the practice of objective medicine—that is, "real" medicine—and the article is "from a thesis submitted to the University of St. Andrews for the degree of doctor of medicine." So its shortcomings—if any—are worthy of examination.

In his second paragraph he says: "The family doctor . . . through lack of training has not the knowledge, and too often not the inclination, to attempt to deal with the obviously neurotic patient." I would humbly ask, without knowledge how can the family (or any other type of) doctor deal with the neurotic patient, so why throw in the slurring words about the lack of inclination? With reference to paragraph five, would Dr. Rorie to-day like to name the medical schools—in Britain—that attempt to supply the opportunity to obtain the aforesaid necessary "knowledge"? I do not ask Dr. Rorie to place these schools in order of merit. With reference to paragraph seven, how does Dr. Rorie propose to rectify the persisting Victorian disapproval? Does he suggest that it is the G.P.'s job? With reference to paragraph ten, which begins, "It is obvious that if the general practitioner refuses, consciously or otherwise. . . ." Please, please Dr. Rorie how can the G.P. refuse unconsciously (=otherwise)? This brings us back to the G.P.'s faulty teaching and (I hope) forces us to consider who is responsible for it.

In his last paragraph but one Dr. Rorie says there is a very strong case for a "small psychiatric unit" in all general hospitals. I could not agree more with this modest requirement, which nevertheless may not come into action for a long time yet because the time lag is at the very top—that is, in the medical schools—as Dr. Rorie himself says. Another reason is that the "small psychiatric unit" will carry, or force, a good deal more with it—for example, there is just as much need for psychiatric

social workers, men and women, as there is need for midwives, district nurses, and such others as the welfare officers of local authorities. These trained (when they are trained) people need not be quite as expensive as registered medical practitioners, but in the effectiveness of their particular jobs of work can be just as useful.

Meanwhile, such ideas carried into co-operative effort will set free your G.P. and you will have every right to demand that he (or she) should be fully trained in knowledge of the job he has to do. The giving of a "merit award" to a G.P. worthy of it might be easily as practicable as the administration of merit awards in the present circumstances to other parts of the medical profession. Finally, if this country wants the general medical practitioner to survive, his training policy cannot be allowed to remain in the state indicated by paragraph five of Dr. Rorie's article. How can anyone expect a "doctor" to become interested in a part (an abnormal part) of real life that he is without adequate knowledge of? Even though I appear to see some related matters in a way not covered by Dr. Rorie's article, I sincerely congratulate him on it.—I am, etc.,

Mansfield. JOHN MCNAMARA.

Psychosomatic Appendicitis?

SIR,—Dr. J. W. Weston (*Journal*, May 7, p. 1158) states that he has had recurrent attacks of mild appendicular colic, and apparently has made a self-diagnosis on the assumption (a prevalent mistake) that pain produced in the appendix is situated in the right iliac fossa. That tenderness and, secondarily, pain in the right iliac fossa do occur in both the inflammatory and obstructive types of appendicitis is well recognized—if the appendix is in the normal site. But the excitation of pain in that situation is produced not in the appendix: it is caused primarily by stimulation of the somatic nerve afferents of the parietal peritoneum, and not by "overaction of the sympathetic." Since the appendix, like the rest of the gut, has a bilateral nerve supply through the autonomic system, it necessarily follows that pain produced in any part of the intestine will be situated in the midline and at a definite site—epigastric, umbilical, or hypogastric—depending on the embryonic position of the segment of gut at fault. On the other hand, pain produced in a bilateral organ (or tissue) is always unilateral, since the innervation is unilateral—e.g., kidney, testis, arm, leg, etc.

Dr. Weston would be wise to "wonder" a little longer and to consider other possible causes for his attacks of "sharp stabbing pain localized to the right iliac fossa" before having his appendix removed.—I am, etc.,

Dundee. F. R. BROWN.

Ban on Heroin

SIR,—Your report under the heading "Medical Notes in Parliament" in the *Journal* of May 7 (p. 1163) makes me write to you again on this subject. You have published several letters in which the ban on heroin is deplored for one reason or another. The writers of these, and the host of doctors who are in agreement with their views, must think that the Association has taken no action in the matter, if Lord Haden-Guest can assume that "the whole medical profession, so far as could be ascertained, was behind the Order" and Lord Mancroft can say "the vast weight of evidence was in favour of the move."

The Association received last year from the World Medical Association a questionary on the subject of the ban on the manufacture of heroin. This was referred to the Science Committee, who recommended as follows: "That the World Medical Association be informed that it is the duty of the Government to legislate against misuse of heroin, but the medical profession should not in any way be deprived of the use of this or any other drug which may assist in the treatment of patients." This resolution was endorsed by the Council of the Association in November, 1954. Seeing that the overwhelming majority of medical men are members of the Association the statements of Lord Haden-Guest and Lord Mancroft were singularly uninformed. Lord Haden-Guest, being a doctor, should have found out the Association's view on the matter before making such a statement.

This is not the first time that the opinion of the Association has been entirely ignored by the Central Health Services Council in recommendations to the Minister, which seems strange seeing that the chairman was recently President of the Association. I am sure it would give satisfaction to members if the Association's views were made clear, possibly by the Public Relations Officer, on occasions such as this when the Government takes a decision contrary to the expressed view of the Association.

I wish someone would inform me what the "perfectly good substitute is" for heroin—to use Lord Mancroft's words. Is it something known to the Central Health Services Council and the Members of the House of Lords but kept hidden from the small fry in whose hands is the treatment of the patients of this country? Or is it "physeptone"? If the latter, Lord Mancroft is in error in his description of this drug.—I am, etc.,

London, N.W.1. R. HALE-WHITE.

SIR,—One appreciates the good intention behind the ban on heroin, but there are certain aspects of this matter which cannot help causing concern. It is clear from the correspondence in the *Journal* and elsewhere that there is no complete substitute for heroin, and such is my own experience. If there was a substitute, then no one would object at all to the ban, and it is obvious that the Government has been misinformed on this point. As it is, legislation will be brought into effect which will have the direct result of condemning some citizens to suffer pain which could be relieved by this drug. A few people will be asked, therefore, to make this sacrifice for the good of a supposedly larger number of their fellow creatures. Such a policy invokes a principle which has always been regarded as unethical and unacceptable to British Medicine, for it is the same principle under which the Germans carried out their much discussed experiments on human subjects. We have fought strongly to preserve the right to prescribe drugs of doubtful value, and I can only hope that the same effort will be made to preserve heroin until a genuine substitute is available. The fundamental function of clinical practice is to relieve suffering, and no weapon employed to this end should ever be banned, even for the most cogent socio-economic reason.—I am, etc.,

Barnton, Midlothian. A. G. DONALD.

The Changing Face of Medicine

SIR,—I was highly interested to read Dr. C. P. D. Grant's splendid contribution, "Youth Looks at General Practice" (*Journal*, April 30, p. 1049) and your comments (p. 1075), and I entirely agree when he calls the N.H.S. a system "designed to undermine incentive and initiative," a system in which a list of "heads" has to be built up to provide a living wage, a system in which "the G.P. can very easily degenerate into a rather apathetic kind of sorting clerk."

Is it not worth while to learn from excellent insurance schemes working in other countries which provide a system without lists and capitation fees? They offer individual services rendered by G.P.s and paid for according to an approved national scale of fees. Minor surgery, treatment of fractures, suitable laboratory investigations, some physiotherapy, all within the capacity of the G.P., could easily be done in G.P. surgeries and paid for accordingly. What an incentive for the G.P. to treat the patient and not to transfer them much too readily to overcrowded out-patient departments. It would mean saving of money and working time for patients sent to such departments, relief of overworked out-patient department personnel, saving of salaries and manpower of nurses so short in supply, clerks, secretaries, physiotherapists, porters, etc. Costs for ambulances and hospital cars would be greatly reduced.

Specialists' services could be changed to bring at the disposal of patients specialists not only for domiciliary visits but also for consultations in their own consulting-rooms, where certain treatment could be provided. Patients would be pleased to have their self-chosen specialist, who would be paid according to an approved scale of national fees.

By abolishing lists and capitation fees I, as a middle-aged G.P., could envisage an easier entry of the young generation into general practice.—I am, etc.,

Finchley, N.3. H. SIMON.

SIR,—My own reactions to eighteen months in general practice differ slightly from those expressed in Dr. C. P. D. Grant's excellent article "Youth Looks at General Practice" (*Journal*, April 30, p. 1049) and Dr. G. F. G. Marshall's letter (*Journal*, May 7, p. 1153). My feeling has been that the many differences between hospital work and general practice all spring from the fundamental one that in hospital jobs we were one of many who played a part in the treatment of the individual patient, whereas in general practice we are alone in representing the medical profession to him. I was just as conscious of these differences as Drs. Grant and Marshall, but I cannot agree with them that this experience of itself constituted an adverse criticism of the undergraduate curriculum.

There is no alternative, as I see it, to the ironical fact that to learn general practice one must first become a general practitioner. One's ingenuity in the application of general principles of both medicine and common sense was certainly taxed to a degree at first, but I never found my basic knowledge so lacking as to be in fear of making a serious error. Occasional reference to a picture book of skin rashes and a small handbook of prescribing was of particular help at first. Harvey Cushing once wrote that every patient presented two questions: first, what can be learnt from him, and secondly what can be done for him. How true to the newcomer to general practice! I personally found the problem of explanation to constitute the greatest difficulty, especially in the giving of a judicious forecast as to the course an illness might take and its likely duration. One can so easily be held to account for any unexplained sequelae when one lives in patients' midst.

Drs. Grant and Marshall both allude to the question of satisfaction of work in general practice. As Dr. Grant says, the tendency to apathy to clinical matters and over-concern with "the practice" as a business entity is a real danger as years go by. This can hardly be conducive to happiness, as no doubt Osler would have told us. I am hesitant in agreeing with the stress which Dr. Marshall lays on the approval earned of patients as a central, reliable source of satisfaction. It is pleasant indeed to bask in the knowledge of this state, and yet, if we do, it is all too easy with time to cease self-criticism and for our clinical standards consequently to fall. As I see it, we can only be sustained in our relative intellectual isolation by keeping alive the scientific approach to problems nurtured in our hospital days by continued reading, especially of symposia which review current thought. As in other facets of life, we have to live on a vision, and much effort is constantly required if it is to remain bright in our minds. It is in this sphere, and the occasions on which my patients have derived benefit in advice or treatment as a direct result of my reading, that I have found the greatest satisfaction of all.

Such an approach, as the mainspring of our thought and work, can do much to help us restore the prestige of general practice to its rightful place in medicine and our own self-respect as professional men. Dr. Grant's suggestions about the introduction of general-practitioner clinical assistantships, and access to *x*-ray departments and pathology laboratories, would help greatly in this motive, and I very much hope will be introduced in due course. George Eliot epitomized this approach in her *Middlemarch*: "I should never have been happy in any profession that did not call forth the highest intellectual strain, and yet keep me in warm contact with my neighbours. There is nothing like medicine for this: one can have the exclusive scientific life which touches the distance, and befriend the old fogies of the parish too."—I am, etc.,

Heswall, Cheshire. D. S. CRAIG.

SIR,—I feel that many of the statements in Dr. C. P. D. Grant's article "Youth Looks at General Practice" (*Journal*, April 30, p. 1049) should not go unanswered. I qualified just before the late war and have been in practice some seven years, five of these in my own single-handed practice, and feel sure that his attitude on many things is not typical of the less senior general practitioner.

He complains of the "volume of trivial complaints." The only objective study on this point that I have seen considered a disease serious when it embodied a major threat to life or livelihood. On this basis, in a London practice of over 3,000, 16% of diagnoses were of serious disease, and the work involved in dealing with these patients was 43% of the total work in the year. In my experience much disease that does not embody such a threat is serious enough to the patient, and difficult and interesting to treat. As for "trivial illness," much serious illness begins in this way, much is a symptom of serious underlying psychological or social trouble which the good doctor must treat, and the remainder gives a good opportunity for health education of a valuable kind.

Dr. Grant deplores "the cessation of clinical control of patients removed to hospital under the National Health Service." What does he suppose happened to these patients prior to 1948? If they did not in fact go to hospital, could they afford to pay doctors and nurses to look after them elsewhere, and were the doctors satisfied that all the resources of medicine were available for their patients in these circumstances? Surely the truth about the increased demand for hospital beds is that now millions of people have a family doctor who never had one before, and that much chronic illness which before was endured in silence is now diagnosed and treated.

I agree very much with Dr. Grant that family doctors should be able to get many investigations done without referring the patient to hospital. (It seems that the co-operation of the Northern Ireland Hospitals Authority puts us in Northern Ireland in a privileged position in this respect.) Much more co-operation between hospital and general practice would be of great advantage to both—and to the patient; but many general practitioners would feel that their work lay in their practices rather than in doing hospital work described as "routine" and not needing "very advanced or specialized knowledge." Many general practitioners seem to feel that because they do not work in hospital they are cut off from all that is really interesting and important in medicine. This mistaken attitude has its origin in methods of medical education; the student has to be taught about disease largely as it is seen by specialists in hospitals. Lay misconceptions about medicine are reinforced, and the drama of the operating theatre, the laboratory, and the *x*-ray departments has come to be regarded as the occupation of every medical man who does a worthwhile job. This produces the attitude of mind which causes Dr. Grant to refer to "the malingerers and neurotics—the pests, the 10% hard core of every doctor's list." It is true that even to-day the undergraduate receives inadequate training in psychological medicine, but that does not justify the description of sick people as pests and malingerers.

However thankful we may often be for the resources of our hospitals and the wisdom of our specialists the practice of medicine is coming more and more into the patient's home. An emergency tracheotomy or intubation for laryngeal diphtheria was a dramatic event, but prophylactic immunization is preferable. Lobectomy for bronchiectasis, or localization and removal of a complicating brain abscess, are remarkable and admirable processes; but prevention of pertussis and early treatment of pneumonia are more acceptable to the patient. Cardiac surgery can mean new life for a cardiac cripple; good general practice in many cases could forestall the development of rheumatic carditis. These are only the most obvious instances; and every year medical progress increases the possibilities of the family doctor's work.

Dr. Grant speaks of "the young practitioner, excluded from the hospital and committed to his desk by the system. . . ." Desks were not unknown previously, and a careful history taken behind one by a doctor who knows his patient as a person often gives more useful information

than a sheaf of special investigations. I prefer to think of the family doctor not as excluded from the hospital but as having the great opportunity of living among his patients, observing them in health and disease, in their homes and at their work, following the natural history of each condition from origin to cure, or as it accompanies each patient to the inevitable end, however long delayed. The opportunities for clinical work and even for research in general practice are very great. Exceptional men have taken advantage of this in the past, and will again in the future. This needs saying again and again, because there is a fashion now for thoughtless general practitioners to belittle their work and to bemoan their "loss of status." I am in complete agreement with Dr. Grant's final sentence: ". . . taken seriously and practised conscientiously it [general practice] is the most difficult specialty of all."—I am, etc.,

Belfast. R. P. MAYBIN.

REFERENCE

1 Backett, E. M., *et al.*, *British Medical Journal*, 1954, **1**, 109.

SIR,—Your report (*Journal*, April 30, p. 1045) of the 1954 presidential address to the Edinburgh Obstetrical Society by Dr. Clifford Kennedy states, "and then two years in the Services, when the mind of the doctor, so far as things medical are concerned, might in the average case be a complete vacuum." Surely this is an *ex cathedra* statement which in fairness to the Services, and the Army, in which I served, in particular should not be allowed to pass unchallenged.

In the first place, doctors, like other people, are called up to meet the needs of the nation, and not specifically to further their personal ambitions. Secondly, despite this fact, experience shows that if any show professional leanings or initiative their place in the professional orbit of the Service is assured. Lastly, I feel sure that the number of Service medical officers who, on transfer to part-time service, can honestly say that they have derived little or no benefit professionally during their time in the Forces must be very small.—I am, etc.,

London, S.W.1. MALCOLM ROBINSON.

Difficulties of Child Adoption

SIR,—Dr. P. M. Fea's letter (*Journal*, April 30, p. 1096) indicates a grave lack of appreciation of the many problems involved in child adoption, and the consequent need for safeguards to protect the child from unwise placement and the adoptive parents from the tragedy of failure. The suggestion that the unwanted child must "justify its existence" implies that the child has incurred a debt to society only to be discharged by the satisfaction of the emotional needs of others, whether these be suitable or not as adoptive parents. The adoption societies are at the present time in a position to select from many applicants. Far from having "an unfounded suspicion" of would-be adopters, experience has shown that there are many considerations other than the fact that a couple may be "kindly disposed." So long as there are younger couples wanting a child it does not seem unreasonable that 40 is usually the upper age limit for adoptive parents.

Some emotional disturbances are exhibited by a proportion of adopted children, and such disturbances are often intensified when the parents are elderly, and particularly when the child reaches adolescence. Children are normally placed in infancy, when they have the best chance to settle in their new home. The later the age of adoption the greater is the chance of behaviour disorders. Dr. Fea, and others who are concerned with these questions, would find that they are discussed by Kornitzer[1] and the Home Office report on adoption.[2]—I am, etc.,

Beckenham. LORNA M. BRIERLEY.

REFERENCES

1 Kornitzer, M., *Child Adoption in the Modern World*, 1952. Putnam, London.
2 *Report of the Departmental Committee on the Adoption of Children*, 1954. H.M.S.O., London.

Measles

SIR,—Your leading article (*Journal*, April 23, p. 1018) deprecates the prophylactic use of sulphonamides and penicillin as routine treatment of measles. During the January–March epidemic this practice has had approximately 50 cases of true measles, ranging from 1 year to 7 years, and in all cases we prescribed sulphonamides or penicillin. There was only one instance of complication, which was in a child of 5 years who developed bronchopneumonia and right-sided otitis media; this case occurred when the mother had not followed our instructions to give the prophylactic treatment.

It would be interesting to know the incidence of complications with or without prophylactic treatment. It appears that there is a definite place for routine prophylactic treatment in measles, starting in the pre-rash stage as soon as the catarrhal symptoms appear and there is a history of recent measles contact. I wish to thank my principal, Dr. R. G. Wigoder, for permission to record these results.—I am, etc.,

London, S.E.6. J. F. LUND.

The Foot as a Half-dome

SIR,—I was especially interested in Dr. J. McKenzie's article (*Journal*, April 30, p. 1068) in which he compares the foot to a half-dome, as it is a concept that I myself found most useful in explaining the mechanics of the foot. But why does he, in common with so many others, describe the forefoot as being pronated when the foot has adopted a "flat-footed" attitude? When the foot is allowed to collapse from the active fully arched posture into a resting or flat-footed attitude, no movement of the forefoot takes place relative to the ground, for it remains plantar grade throughout. Hence it is certainly not pronated relative to the ground. But in this position the back part of the foot has "rolled in" into a valgus or everted position, and since the forefoot has not moved it must now be in a position of inversion in relation to the rest of the foot, and inversion is synonymous with supination. In the flat-footed stance the forefoot is thus supinated relative to the back part of the foot. Thus the change from the fully arched to the relaxed flat-footed posture is brought about primarily by rotation about an antero-posterior axis of the front and back parts of the foot in opposite directions. It is for this reason that I like to refer to the foot in the relaxed posture as being "unscrewed" rather than flat, and "screwed up" when it adopts the fully arched active position.—I am, etc.,

London, S.E.1. T. T. STAMM.

Influenza

SIR,—Even in the face of an epidemic of influenza it is well-nigh impossible these days to differentiate such cases from other respiratory viral infections without routine serology in every case, as suggested by Dr. John Fry (*Journal*, February 19, p. 478). It is equally impossible to assess the true incidence of pulmonary opacities without radiological investigation of the chest in every case, and, for many reasons, that cannot normally be countenanced.

In the first half of 1953 (influenza virus A year) the Army Chest Centre, Connaught Hospital, Bramshott, was asked to deal with the overflow of mild cases of upper respiratory tract infection from other hospitals. Five hundred cases were admitted as upper respiratory tract infection between January 15, 1953, and May 5, 1953. Every case had a radiograph of the chest on admission, and the incidence of pulmonary opacities was most revealing. Routine serology (see Table) was carried out in all such cases and in random cases amongst the remainder. The cases were classified as follows: infectious mononucleosis, 6; rheumatic fever, 1; rubella, 1; tuberculous primary pleural effusion, 1 (A. and A.F.B. isolated on culture); transverse myelitis, 1; herpetic stomatitis, 1; malaria, malignant tertiary, 1; scarlet fever, 1.

The remaining 487 cases were then divided into the following groups, which are as defined by Stuart-Harris[1] but with certain modification. The figures in parentheses give the number with pulmonary opacities: *Group One.*—Common cold, 8. *Group Two.*—Bacterial sore throat, 112 (1). *Group Three.*—Febrile catarrh with exudate, 47 (4). *Group Four.*—An influenza-like illness with (*a*) no evidence of catarrh, 51 (1); (*b*) minimal catarrh, 67 (16); (*c*) marked catarrh, 202 (44). All groups were easily recognized, and therefore the high and accurate incidence of pulmonary abnormalities demonstrable on routine radiological examination of the chest in every case on admission is of particular interest—for example, Group 3 plus Group 4 (*a*), (*b*), and (*c*): 65 out of 367 cases, or 17.71%; Group 3 plus Group 4 (*b*) and (*c*)—that is, all cases with catarrh: 64 out of 316 cases, or 20.2%—that is, 1 in 5; Group 4 (*b*) and (*c*); 60 out of 269 cases, or 22.3%—that is, more than 1 in 5.

	Total Cases	Serology Tested	Influenza "A"	Influenza "B"	"Q" Fever	Psittacosis L.G.V. Group of Viruses	Streptococcus MG Agglutinins	Negative Serology
Group 1 ..	8	—	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
„ 2 ..	112	7 (1R)	—	—	—	—	—	7 (1R)
„ 3 ..	47	10 (4R)	—	—	—	—	—	10 (4R)
„ 4(*a*) ..	51	6 (1R)	2 (1R)	2	—	—	—	2
„ 4(*b*) ..	67	24 (16R)	7 (3R)	3 (3R)	—	2 (2R)	—	12 (8R)
„ 4(*c*) ..	202	61 (43R)	16 (10R)	12 (9R)	1 (1R)	2 (2R)	—	30 (21R)
Total ..	487	108 (65R + 1R AWOL)	25 (14R)	17 (12R)	1 (1R)	4 (4R)	—	61 (34R)

R = With radiological changes. The case who went A.W.O.L. did not have serological tests carried out.

These results are of outstanding interest because such a rate of pulmonary complications demonstrable on chest radiography is by no means generally recognized. Such results would be of special significance to those with Service experience, who know that anyone with a febrile illness of at least one day's duration is likely to be admitted to hospital. The radiological changes were those found in respiratory virus infections but are not diagnostic of, or peculiar to, any one virus. The term "adhesive bronchial pneumonia" is both descriptive and accurate and should replace the term "aspiration pneumonia," which is apt to be so readily used in such cases.

These brief remarks are part of a paper on the subject of upper respiratory tract infection which it is hoped to publish in the *Journal of the Royal Army Medical Corps* in due course. The authors of this work include Captain C. H. Jones, R.A.M.C., and Captain J. G. Elliott, R.A.M.C. —I am, etc.,

Hindhead, Surrey. JOHN MACKAY-DICK.

REFERENCE

[1] Stuart-Harris, C. H., *Influenza*, 1953.

Exchange Transfusion in Haemolytic Disease of the Newborn

SIR,—The article by Drs. William Walker and Sheilagh Murray on the treatment of haemolytic disease of the newborn (*Journal*, July 17, 1954, p. 126), claiming a mortality rate of 2%, and reiterated in a further article by Drs. Walker and G. A. Neligan (*Journal*, March 19, p. 681), cannot be allowed to pass without comment.

Admirable as is the work of the Durham school on this subject, they lay themselves open to the criticism that by ignoring stillbirths when computing their mortality rate they have rendered their figures worthless, since all of the worst risks will have been eliminated before birth, and the mortality rate for the less severely affected liveborn infants becomes unfairly bettered. Furthermore, in the matter of excluding the deaths of several of the liveborn infants in the 1955 report, it would seem that the liveborn mortality rate is also questionable. For example, two of the infants (K. and P.) amongst the group III cases, whose death was not attributable to haemolytic disease, had cord blood Hb values of 8.0 g.%, while one of them (K) had a serum bilirubin value of 15 mg.%. This alone, according to Dr. Walker's own published standards, should signify a severe degree of disease, severe enough *per se* to cause the death of many infants. Yet he has excluded them from the mortality figures on the grounds of double pathology. He has *included* in his mortality figures a much less severely affected infant (H.) in group III whose cord Hb value was 10.3 g.% and bilirubin only 1.9 mg.%.

To the critical observer such inconsistencies render the figures quite unacceptable, but one might well ask what should or should not be included on the grounds of double pathology, because who is to judge just where to draw the line? It is a simple matter, by excluding cases on the grounds of other causes of death, to make one's mortality rate just what one likes. Indeed, the post-mortem results of many of Dr. Walker's cases showed just exactly nothing, or ? heart failure. Hence, if the necropsy revealed nothing, the death was presumed as due to haemolytic disease; if any other pathological cause can be found, haemolytic disease is excluded.

The only really scientifically honest way to arrive at approximate mortality figures is to include all stillbirths and all neonatal deaths of infants whose erythrocytes show a positive direct Coombs test. This may be difficult in the case of macerated stillbirths, but we have in this hospital counted all stillbirths (after 28 weeks) of infants whose mother's serum contained abnormal antibodies. Usually the presumption of incompatibility becomes almost a certainty when the previous history is consulted or there has been an undoubted change in maternal antibody titre. The stillbirth rate by this means may be slightly too high, but the figure must be closer to the truth than that obtained by ignoring these cases.

It is unfortunate that these British workers have decided to write off their erythroblastotic stillbirths as irretrievable on evidence which is not even statistically significant.[1] Premature induction of labour, as a means of saving at least a proportion of these affected infants, has been banned on unacceptable evidence. The incidence of kernicterus in premature infants is reputed to be higher than in mature babies, and this is also debatable. It is more probable that it is not prematurity itself which contributes to kernicterus, but the way in which the babies are treated and handled. Evidence to substantiate these remarks is shortly to be published, and the plea is advanced to those interested workers to keep an open mind before accepting the dictum that "premature induction of labour has no routine place in the management of this disease."—I am, etc.,

Subiaco, Western Australia. G. A. KELSALL.

REFERENCE

[1] Mollison, P. L., and Walker, W., *Lancet*, 1952, 1, 429.

Coal-workers' Pneumoconiosis

SIR,—I have read with great interest and appreciation Drs. J. C. Gilson and G. S. Kilpatrick's article on coal-workers' pneumoconiosis (*Journal*, April 23, p. 994). They have given a lucid summary of a difficult social and therapeutic problem. They discuss the nature of chest pain in these cases, and I would like to quote some of the symptomatology I have elicited from Durham miners with pneumoconiosis.

Assessment of pain is always difficult, and especially so when the question of pension is involved. When one has excluded the more obvious causes of pain such as strain, cough fracture, or pleurisy, there remain a number of more obscure cases which often present some of the following features. The pain may be retrosternal, in either pectoral region, or be right across the front of the chest, and is often related to effort. In character it may be constrictive. If this is the only history obtained, cardiac ischaemia cannot

be ruled out without an E.C.G. before and after exercise. But usually the pain presents other features. For instance, it may be periodic, coming on for a few days or weeks at a time, though not continuously present. When the man is having a bad period the pain may not be related to exertion, but may occur in bed at night or while sitting in the armchair. When related to exertion the pain may be relieved by rest, but often persists for hours before this occurs. During the periods of remission the miner may be capable of considerable exertion. The pain is often associated with dyspnoea, more rarely with wheeze.

What such pain is due to is not clear. I have seldom attributed it to cardiac ischaemia because there are so frequently atypical features. Emphysematous bronchitics may get similar pain, but it seems a much more dominant feature in pneumoconiosis. Perhaps repeated undiagnosed pleurisies are related to the cause. I should be interested to learn if the above description of chest pain in pneumoconiosis fits in with the findings of Drs. Gilson and Kilpatrick.—I am, etc.,

Sunderland. H. R. THOMSON.

Chlorpromazine

SIR,—The report by Dr. J. R. Tasker (*Journal*, April 16, p. 950) of a fatal case of agranulocytosis, due to chlorpromazine, clearly puts the drug in a new category. My note (*Journal*, April 23, p. 1034) concerning the use of the drug in a few cases of severe and otherwise intractable vomiting of whooping-cough was by then already in the process of printing, and it invited the obvious rejoinder by Dr. J. H. Owen (*Journal*, May 7, p. 1155).

The fact remains that whooping-cough is at present in this country one of the chief killing diseases of childhood, with an impressive respiratory morbidity in later adult life. Chlorpromazine, as a drug powerfully effective in controlling the paroxysms and vomiting of this potentially lethal and disabling illness, is worthy of a controlled group trial in a selected number of severe cases as short-term therapy. The general practitioner will see but few cases of this type even in an epidemic. If this correspondence stimulates a more extensive investigation, it will have served its purpose.—I am, etc.,

London, S.E.13. HOWARD REEVE.

Cyst Formation Following Hernia Repair

SIR,—It would be a pity to allow Mr. G. T. Watts's rather sweeping condemnation of the method of hernia repair by skin implant (*Journal*, May 7, p. 1156) to pass unchallenged. I have used the method now for 10 years, restricting it to difficult cases where a satisfactory repair from the tissues locally available appeared impossible—recurrent herniae, incisional herniae, about 100 cases in all—and have been very pleased with it. I have had no cysts, no serious sepsis, and few recurrences. In many of the cases the defect was large and the implant was the only bar to recurrence—for example, a man who had a hole blown in his abdominal wall by the discharge of a 12-bore sporting gun at a range of one yard (0.9 m.). In one case I had to reopen the abdomen three years after repairing a ventral hernia and was impressed by the thick shining tendon-like tissue which had replaced the skin implant.

The development of cysts implies that the skin has been placed under conditions which allow the survival of epithelial elements. I think the way to avoid this is to make sure that the skin is sutured everywhere under full tension in all directions, and especially that no little folds or loose corners are left at the edges of the implant. This is difficult and time-consuming and makes the operation a little tedious. I suspect that some of the cysts that occur may be due to modifications of the method introduced in a misguided attempt to make it easier or quicker. I am sure that if used only for the sort of case I have indicated, and carried out with care, the method will be found more successful than the alternatives of repair by fascia lata or by the implantation of some foreign body.—I am, etc.,

West Hartlepool. W. IRVING.

Natural Childbirth

SIR,—This subject, whenever it is discussed, invariably discovers ardent adherents, equally passionate dissentients, and much confusion between antenatal exercises, antenatal preparation for pregnancy, labour, and the puerperium, and relaxation exercises. Would it not be wise to admit that there is little to be said for antenatal exercises in relieving the discomfort and shortening the duration of labour, but that they do prepare the woman for the very valuable exercises she will, if she is wise, practise after delivery?

Antenatal preparation has, of course, a great deal to be said in its favour, for the average primigravida is sublimely ignorant of the problems ahead, has probably acquired a great deal of horrific and incorrect information about the pangs of labour, the travail of childbirth, and so on from friends and relatives, who become surprisingly sadistic at such times, and is almost certainly scared about some aspect of pregnancy, in particular labour. Intelligent advice and correction on all these matters is obviously part of good antenatal preparation for natural childbirth, but what is "natural childbirth"? Presumably it means an unassisted delivery with no pain, at most only discomfort, and this question of pain is really what all the correspondence is about.

Dick Read's contribution to the problem is his reiteration of the well-known fact that tension begets pain, or, rather, lowers the pain threshold; and the essence of natural childbirth is preparation for a natural process. Not every woman can be assured of freedom from discomfort when she is having a baby any more than when she is having a tooth drilled. Her appreciation of pain can, however, be lowered by previous preparation, pain-relieving drugs, or frank anaesthesia, and the first may be enough or the last necessary. The experienced general practitioner is perfectly well aware of this, and when looking after a young primigravida he first gains her confidence, explains the problems she must face, and, in fact, with continuing supervision does everything to relieve tension and anxiety. When she goes into labour his steady voice and confident assurance are powerful and continuous aids towards "natural childbirth." Unknowingly he may induce a state bordering on hypnosis, and with some cases a completely painless labour follows. The essential factor is surely the confidence the woman has in her attendant, and obviously antenatal preparation must encourage it. Relaxation exercises, conducted by the one who will attend the woman in labour, are all to the good, and good relaxation between contractions may be ensured, but it is useless to promise *every* woman a labour free from pain, and analgesics should never be withheld even by the most enthusiastic "naturalists."

Perhaps if we remember the disservice done to women by referring to "pains," by the publicity given to such items as gas to relieve the anguish of labour for every woman, "'trilene' now safe for midwives," and so on, and tried rationally to present the problem, and promote relaxation fairly and try to relieve tension, natural childbirth might and could be more commonly achieved, even in highly organized maternity units.—I am, etc.,

Pembury, Kent. E. D. GRASBY.

Ante-partum Haemorrhage

SIR,—Mr. Frank Stabler's excellent paper on this subject (*Journal*, May 7, p. 1145) will be of great value to the general practitioner in the out-patient management of this condition. I would venture to disagree, however, with one of his recommendations. My colleagues in the pathological laboratory have impressed upon me the importance of providing a sample of blood for cross-matching before the administration of dextran or any of the other plasma substitutes; and in cases where the restoration of blood volume is necessary merely as a preliminary to blood transfusion we have found it is usually preferable to use normal saline rather than dextran. In domiciliary conditions it may sometimes be difficult to obtain a blood sample and then to put

up a dextran transfusion, and for that reason I would suggest that normal saline should be used as a stopgap measure. Although the saline is rapidly excreted from the circulation in normal circumstances, in the collapsed patient it seems to produce temporary improvement for about an hour, which should usually give sufficient time for a flying squad to reach the patient with blood.—I am, etc.,

Worcester. J. A. CHALMERS.

Injection Technique

SIR,—I am grateful to Dr. John Richards (*Journal*, April 30, p. 1092) for drawing attention to the value of stretching the skin when giving injections. That is a point I omitted to mention (*Journal*, April 9, p. 909), and the benefit of which I had not fully appreciated. But surely, apart from assisting penetration of the skin by the needle, does it not supply a further illustration of Pavlov's dictum, that whether the stimulus be pain, touch, temperature, or stretching, the body can only respond to, or sense, one stimulus at one time? Stretching of the skin may be felt during an injection instead of either the touch of the needle or the pain of its prick. The more the skin is stretched, the stronger will be the stimulation of the stretch-sensing nerve endings, and the greater the chance that stretch-stimulation will override and prevent appreciation of pain-stimulation. A quickly given injection affords time for appreciation of one stimulus only—the dominating stimulus. Make sure when giving injections that the dominating stimulus is the pleasant one—stretch or touch—not the unpleasant one of pain.

Based on this principle, here is another simple but effective dodge. When injecting children in the arm, instruct the mother to stroke or rub the child's leg. The dominating stimulus observed by the child is the touch on the leg; the minor stimulus, pain in the arm, escapes its observation—provided the pain stimulus in the arm is reduced from a major to a minor stimulus by employing the procedure which I described in my letter.—I am, etc.,

Reading. K. D. SALZMANN.

Diphtheria Immunization in Guernsey

SIR,—In 1937 an epidemic of diphtheria started in the autumn, reached its peak in the winter and autumn of 1938, and subsided in 1939. In 1938 the Guernsey Board of Health proposed that there should be a law for the compulsory immunization of all children between 1 year of age (afterwards changed to 2 years) and 10 years of age, without any conscience clauses for exemption. Exemption could be obtained for ill-health, previous attack of diphtheria, or a negative Schick test, subsequently all children to come under the law on reaching the age of 2 years. The *Projet de Loi* was passed by the States of Guernsey in June, 1938; this was confirmed by Order in Council in March, 1939.

A campaign for voluntary immunization was carried out until the law came into force, and 40% of children under 15 years of age had been inoculated by January, 1939; by the end of 1939, 7,600 children (76%) had been inoculated. A large number over the age of 10 years had been immunized voluntarily. In 1940 approximately 8,000 children out of the 10,000 under 14 years of age were evacuated to Britain, and in June the island was occupied by the Germans. Supplies of A.P.T. and T.A.F. could no longer be obtained, and immunization was suspended until liberation in May, 1945. Then all children between the ages of 2 and 7, which covered the war years, not previously immunized, came under the compulsory law. Subsequently all children in Guernsey come under the law as they become 2 years of age, and in practice more than 95% of these children are immunized. Children not traced, children who come to live here after 2 years of age or exempted for ill health, account for the remainder. Free voluntary reinoculation is offered, and since 1945 approximately 40% have accepted this. The injections are carried out by the local medical practitioners. No serious ill effects from the injections have been reported.

When the law was proposed in 1938 there was considerable opposition, but since the war this has died down, and even individual objection on principle is very rare, although pressure has to be brought on a certain number of parents due to their inertia.

I give below the numbers of notified cases of diphtheria for the years 1897 to 1954, with the population at certain years.

Year	Notified Cases of Diphtheria	Population	Year	Notified Cases of Diphtheria	Population
1897	35	37,242	1927	33	
1898	122		1928	61	
1899	121		1929	57	
1900	80		1930	37	
1901	66	40,300	1931	32	
1902	179	(census)	1932	11	40,478
1903	107		1933	6	(census)
1904	50		1934	4	
1905	40		1935	3	
1906	125		1936	1	
1907	94		1937	62	
1908	48		1938	489	
1909	37		1939	192	
1910	65		1940	11	
1911	117	41,854	1941	1	33,500
1912	163	(census)	1942	5	(average)
1913	72		1943	—	
1914	45		1944	—	
1915	28		1945	2 (average)	
1916	6		1946	4	25,500
1917	8				(average)
1918	14		1947	2	38,000
1919	8				(estimate)
1920	86		1948	—	
1921	278	37,914	1949	3	
1922	179	(census)	1950	—	
1923	122		1951	2	43,547
1924	172		1952	1	(census)
1925	216		1953	—	
1926	101		1954	—	43,414 (estimate)

—I am, etc.,

Grange, Guernsey. ROWAN REVELL.

POINTS FROM LETTERS

Analgesia for Tooth Extraction

Mr. HERBERT CAIGER (Banstead, Surrey) writes: The following simple method of securing almost painless extraction seems worth putting on record. A dentist in Kimberley used it when extracting a lower molar of mine some 60 years ago. . . . I used it very frequently for 20 years in country practice in South Africa, where dentists were not always available. Swabs of cotton-wool are soaked in a mixture of equal parts of tinct. aconit. and chloroform and applied, one on the inside and one on the outside of the gum, for about three-quarters of a minute, with a larger dry swab covering each. The numbing and burning sensation produced almost completely obliterates the pain of extraction. This simple technique . . . is available without an anaesthetist; it is less painful to the patients than injection into the gums, and probably less costly; and available when more modern methods are perhaps not so. If possible, the tinct. aconit. used for the mixture should be made with rectified spirit like that in the *Pharmacopoeia* of 1885—not like the later tincture made with weaker spirit and mixing less perfectly with the chloroform.

Speaking Up

Dr. J. B. GURNEY-SMITH (Redhill) writes: I read with considerable interest the two recent letters on this subject and venture a few observations. I agree with Dr. J. Hamilton McIlroy (*Journal*, April 2, p. 853) in his plea for instruction in voice production for medical students. Comparatively few in our profession are blessed with polished articulation, as is apparent after attending a sectional discussion of any medical society. Medicine is one of the three great learned professions, and it is obvious that a doctor is liable to be involved in situations requiring public utterances from time to time. I feel no doctor, however learned he be, should be invited to deliver lectures and addresses unless he knows how to "deliver the goods." As an Anglican lay-reader, who frequently conducts services and preaches in churches of varying size and of diverse acoustic properties, I can vouch for my views. I would like to pass on two simple tips which are very important—that is, (1) look at the back row in speaking and then everyone in between will hear, (2) maintain an even volume of tone throughout the delivery. How many speakers and even clergy drop their voices at the ends of sentences and so one misses the last few words, which may be vital.

Obituary

JOHN LOWE, C.B.E., *M.C.*, M.D., F.R.C.P.

Dr. John Lowe, medical secretary of the British Empire Leprosy Relief Association and honorary secretary of the International Leprosy Association, died suddenly in London on May 13.

Born at Handsworth, Birmingham, in 1898, John Lowe attended King Edward's School, Birmingham. After service in the first world war, during which he won the M.C. in France, he studied medicine at Birmingham University, graduating M.B., Ch.B. in 1922. A year later he went out to India as a medical missionary in the Leprosy Home at Dichpalli in the Nizam's Dominions. While there he obtained the M.D. for a thesis on malaria. In 1931 he joined the leprosy research department at the Calcutta School of Tropical Medicine, and became head of the department in 1935. For a number of years he acted as assistant editor, and later as editor, of the *Indian Medical Gazette*. During the second world war he was appointed professor of tropical medicine and director of the School of Tropical Medicine at Calcutta. For his work on leprosy he was awarded the Kaisar-i-Hind Gold Medal in 1944.

In 1946 Lowe retired from his appointments in India and in the following year, after obtaining the M.R.C.P., went out to Nigeria. He first worked under the British Empire Leprosy Relief Association, and later under the Nigerian Government at the Leprosy Research Centre at Uzuakoli in the Eastern Province. His energies were chiefly directed towards finding an improved form of treatment for leprosy. He was the first to publish satisfactory results with the oral administration of diaminodiphenyl sulphone. This was found to be effective, safe, and easily administered, while inexpensive enough to be used in wholesale mass treatment. It is now adopted as the standard treatment for leprosy in most countries throughout the world. Lowe published many papers, chiefly on leprosy. He was a clear thinker, writer, and speaker.

Lowe was appointed C.B.E in 1953, and in spite of impaired health he continued to work in Nigeria till he came home in 1954. In that year he was elected F.R.C.P. and was appointed medical secretary of the British Empire Leprosy Relief Association, and undertook also the honorary secretaryship of the International Leprosy Association. But his work was hampered by repeated heart attacks, and in the end it was from one of these he died. He is survived by a widow and two sons, both medical men.

E. M. writes: Dr. Lowe has added much to our knowledge of leprosy, and sufferers from that disease in India, Africa, and indeed throughout the world owe him a debt of gratitude. His death is a sore loss in the field of leprosy research, a field in which there are all too few first-class workers. Low had the true scientific spirit—the desire for truth and the power of self-criticism. While not seeking undue credit for himself, he was always quick to give credit to others whom he considered worthy. In research he was a good colleague to work with. Though sometimes deliberate in getting off the mark, he lost no time once he got going, and threw himself with energy and thoroughness into whatever he had undertaken.

Sir ARTHUR MACNALTY writes: May I be allowed to pay a tribute to my friend and colleague Dr. John Lowe? He was well known as a specialist in tropical diseases, his work in this field at the Calcutta School of Tropical Medicine being outstanding. He did much research in leprosy, and from 1947 to 1954 was in charge of the research unit of the leprosy settlement at Uzuakoli, Nigeria. The British Empire Leprosy Relief Association were glad to welcome him back as their medical secretary, and as chairman of the medical committee of the association I found his counsel and help invaluable. He had done much research on the treatment of leprosy by sulphonamides, and was investigating the use of B.C.G. in prophylaxis of the disease. In spite of ill-health, he battled on, working indefatigably in the campaign against leprosy, although he knew the price might be his own life. I often exhorted him to rest and take more care of himself. His reply invariably was that he preferred to die fighting. He had his wish, and, after a noble and well-spent life, no one could have been better prepared when the summons came to leave this world.

ETHEL CASSIE, O.B.E., M.D., D.P.H.

Dr. Ethel Cassie, who died at her home at Freeland, Oxfordshire, on May 7, was one of the architects of the maternal and child health services of the country. She was 72 years of age. She was best known as the senior medical officer for maternity and child welfare at Birmingham, but her earlier work will be remembered also in Scotland, where she opened the first child welfare centres in Edinburgh more than 40 years ago. Her 22 years in Birmingham brought to the services of that city a more than national repute for the high quality of the administration and practice of maternal and child health work.

Ethel Wiseman was born on September 3, 1882, at Dalhousie, Punjab, India, the eldest child of Frederick Wiseman, of the Indian Civil Service. Her father's early decision that his first child should become a doctor remained unaltered when the first child was a girl, and Ethel Wiseman entered the Edinburgh School of Medicine for Women in 1901. She graduated M.B., Ch.B. in 1906, obtaining the Dorothy Gilfillan Prize as the most distinguished woman student in the university examination, and took the D.P.H. of the Scottish Royal Colleges in 1907. She married Alexander Cassie, a science tutor, in 1907, but the marriage was not finally successful and they parted in 1920. Alexander Cassie died in 1933. Ethel Cassie commenced general practice in Edinburgh in 1908 and was appointed visiting physician to the Hospital and Dispensary for Women and Children. She became medical officer of health of the county and boroughs of Clackmannanshire in 1915 (substituting for the medical officer of health, who was on war service) and assistant medical officer for child welfare in Leith in 1918. In 1921 she was appointed senior medical officer for maternity and child welfare in Birmingham, first under Sir John Robertson and later under Dr. H. P. Newsholme, and continued in this post until her retirement for health reasons in 1943. She proceeded to the M.D. in 1923, and in 1926 gained the Jessie Macgregor Prize for Medical Women, awarded by the Royal College of Physicians of Edinburgh for "the best record of original work in the science of medicine."

It was the quality of originality that made Ethel Cassie outstanding in health administration. She was not one to wait for a lead from others, but rather to give the lead and explore new fields. It was on her advice that the first premature baby unit in this country was opened at the Sorrento Maternity Home in Birmingham 24 years ago. Her understanding of the needs and difficulties of foster children and illegitimate children led to the adoption of special schemes for their care in Birmingham many years before their needs were high-lighted by

the Curtis Committee. Much of her pioneer work has later been embodied in Government circulars to local authorities. She published in 1929 a textbook on maternity and child welfare and contributed also to other publications, but she was not prolific either as a writer or on the platform, preferring always to translate her thought into action rather than words. Her administrative ability and wisdom, coupled with a lively knowledge of clinical medicine, brought her wider responsibilities than local authority work. She was a member of the Departmental Committee on Maternal Mortality appointed by the Minister of Health in 1928, which issued its classic reports in 1930 and 1932. She was appointed O.B.E. in 1941, and in the following year became a member of the Minister of Health's Advisory Committee on Mothers and Young Children. In 1944 she was appointed a member of the Royal Commission on Population, and those who knew her well would discern her influence in its report issued in 1949. Later she took part in initiating a Ministry of Health survey of the growth of infants and young children, but increasing ill-health compelled her to relinquish active work in 1951. Her death will recall to many how much the present high standard of maternal and child health in this country owes to her, not only through her leadership in local authority work but through the stimulus of her constructive thought over a wide field. There was indeed truth in the ancient form of words appointing her—"our trusty and well-beloved Ethel Cassie"—to the Royal Commission in 1944, "reposing great trust and confidence in your knowledge and ability."—K. M. H.

Dr. GEORGIE I. BRODIE writes: With the death of Dr. Ethel Cassie there passes one of the most outstanding and colourful personalities in the field of maternity and child welfare. As her deputy in Birmingham I was privileged to learn from and to be inspired by her. From near and far her pioneer work in the sphere of maternity and child welfare was renowned. Closely working with her, I was daily aware of the bases of that renown. Hers was the mind of a builder, and to the edifice she constructed in Birmingham she brought many talents, not the least of which were a clarity of mind, a singleness of purpose, and a capacity to imbue others with enthusiasm for improving the lot of mothers and children. All workers in the maternity and child welfare field owe much to her for making a model administrative service, which has been copied here and abroad, and rarely improved upon. To her ability as a medical officer Dr. Cassie added a wide range of interests. She was recognized as a connoisseur of old furniture and china. She travelled widely, was a voracious reader, and an interesting conversationalist. Her charm was never more evident than in her own home, where she entertained so delightfully, and those of us who were privileged to enjoy her friendship and hospitality will for long feel the loss of a stimulating and endearing personality. The maternity and child welfare service will always owe a debt of gratitude to Dr. Cassie for her outstanding ability and pioneer work.

J. R. HUTCHINSON, M.D., D.P.H.

Dr. J. R. Hutchinson died on May 6 at Chalfont St. Giles, Buckinghamshire, aged 75. He had retired from the Ministry of Health in 1947 after 36 years' service in the epidemiological divisions of the Local Government Board and the Ministry of Health, of which he became a senior medical officer.

James Randal Hutchinson studied medicine at Owens College, Manchester, and graduated M.B., Ch.B. with honours in 1902. He was awarded the Bradley scholarship for clinical surgery, but was soon attracted to preventive medicine, and took the D.P.H. of Manchester in 1904. His first contribution to public-health literature consisted of papers on the eyesight of Blackburn schoolchildren, which were published in the medical officer of health's annual report for 1907. In 1908 he became senior assistant to that great character Dr. James Niven, medical officer of health of Manchester, and two years later was himself appointed medical officer of health of Wigan. These were busy times and places for a man interested in communicable diseases. He published reports on outbreaks of scarlet fever at Crumpsall in 1909, typhoid from ice-cream in Manchester in 1910, and smallpox in Wigan in 1911. Throughout the period he was intimately concerned with the clinical care of the infectious diseases and particularly tuberculosis, and in 1911 he proceeded M.D., his thesis having dealt with "the presence of typhoid bacilli in enteric fever and afterwards." In this connexion it is interesting to note that in 1943 he published in the *British Medical Journal* a paper on the value of phage typing in the investigation of outbreaks of paratyphoid fever.

Hutchinson was in his 32nd year when, in 1911, he joined the medical inspectorate of the Local Government Board, and he was responsible for several of the reports to the Board which are classic examples of the descriptive epidemiology of that period. He became a master of the subject of the local authority's responsibility for the control of infectious diseases and was typical of that small but strong body of local-government-trained men who provided the backbone of the newly formed Ministry of Health, in which he rose to the post of senior medical officer. He had a fine gift of appraisal and criticism and was a trenchant critic of loose theorizing, sloppy argument, and tendentious conclusions. His fastidious mind was well suited to the pursuit of epidemiology and was matched by his personal characteristics in a remarkable way. His very many friends in the public health service will remember this precision—how neatly the bows on his bespoke shoes were tied and how the bowler hat gave place to the boater on the same day in May each year; how his car was always spotless, and there was rarely a weed in his lawn. These qualities made him a challenging teacher but also a comfortable and loyal companion. One knew where one was with Randal Hutchinson and could rely on his facts and on the soundness of his judgment. Perhaps his most characteristic work was the "Report of the Committee on Vaccination, 1926" which remains as a memorial. His swan song was a historical note on "The Prevention of Smallpox in England," published as an appendix to the Chief Medical Officer's Report, 1946.

Dr. Hutchinson was married and is survived by his widow, to whom we extend deep sympathy in her loss.—W. H. B.

CORNELIUS A. GRIFFITHS, F.R.C.S.

With the death of Mr. Cornelius A. Griffiths on May 7 Cardiff has lost a notable surgeon of the old school. He was 90 years of age. Cornelius Albert Griffiths was born at Merthyr in 1865. He studied medicine at Bristol, where he gained the Martyn Memorial Scholarship in Pathology in 1888 and the Sanders Scholarship in 1889, and at St. Bartholomew's Hospital, London. With the foundation of the University of Bristol still many years ahead and the University of Wales not yet empowered to grant medical degrees, he sat the London Conjoint examination and qualified

in 1889. He then held house appointments at Bristol General Hospital, and from 1890 to 1893 was medical tutor in the Bristol Medical School. In the latter year he obtained the F.R.C.S., and took the post of resident medical officer at the old Swansea General and Eye Hospital. In 1894 he settled at Cardiff and a few years later was appointed honorary assistant surgeon to the Cardiff Infirmary, and surgeon and honorary secretary of the Cardiff branch of the Surgical Aid Society. Later, he became honorary consulting surgeon to the Porth and Maesteg cottage hospitals. During the first world war he worked as a surgeon at the 3rd Western General Hospital, with the rank of major in the R.A.M.C., and after the war he became honorary surgeon to King Edward VII Hospital, now the Cardiff Royal Infirmary. He was a member of the British Medical Association for 65 years, and a justice of the peace for Cardiff for over 30 years.

We are indebted to Professor LAMBERT ROGERS for the following appreciation:

At 90 years of age the death of Mr. Cornelius Griffiths removes from us the last survivor of a little group of octogenarian and contemporary members of the consultant staff of the Cardiff Royal Infirmary. In the last few years they have dropped away one by one: first Mr. Geary Grant, consulting surgeon, then Dr. Cyril Lewis, consulting physician, and Sir Ewen Maclean, at one time President of the Royal College of Obstetricians and Gynaecologists, and professor of obstetrics and gynaecology, and now Mr. Cornelius Griffiths, who outlived them all and who had been a consulting surgeon for many years. Often his slightly stooping, spare figure with its slow, deliberate, and measured tread was to be seen walking along one of the main streets of Cardiff, stick in hand, cigar in mouth, and a soft round hat on his head. Recently his memory had been failing and he would not always recognize whoever addressed him; and more recently still he had been missing from his accustomed haunts and confined to his house. His actions were always deliberate, unhurried, and gentle, as was his operating, for he was a neat, bloodless, precise, and careful operator whom it was a pleasure to watch at work. While he was no great contributor to the literature of his subject, Cornelius Griffiths was a painstaking, careful practitioner of it and was one of that great band of provincial surgeons in this country who, true to high ideals, have done so much to enhance the prestige of British surgery and the high standard of surgical work in the hospitals of our land. His death, like his living and all that he did, appears to have been gentle and dignified. He was revered and respected in Cardiff and South Wales, where he had an extensive consulting practice. He had been retired for so many years that the younger surgeons of to-day knew him not.

A. J. WILSON, M.D., F.R.C.P.Ed.

Dr. A. J. Wilson, who died suddenly on April 30 at the age of 56, was a well-known physician in the Midlands. At the time of his death he was the senior honorary physician and honorary physician in charge of the electrocardiographic unit at the Coventry and Warwickshire Hospital, Coventry.

Arthur James Wilson was born at Whitehaven, Cumberland, on April 3, 1899. From St. Joseph's College, Dumfries, he entered Edinburgh University to study medicine at the age of 16, graduating M.B., Ch.B., with first-class honours, in 1921. A brilliant student, he acquired many prizes and distinctions, including the Wightman Prize in clinical medicine in 1920 and the Pattison Prize in clinical surgery in 1921. He proceeded to the M.D., with honours, in 1928. Obtaining the M.R.C.P.Ed. in 1936, he was elected a Fellow of the College four years later. After graduation Wilson held appointments as house-physician at the Coventry and Warwickshire Hospital and as senior house-surgeon at Salford Royal Hospital, before returning to Coventry to become honorary anaesthetist at the Coventry and Warwickshire Hospital. For a short period he was engaged in general practice in partnership with the late Dr. W. H. Lowman. In 1927 he was appointed assistant physician to the Coventry and Warwickshire Hospital, and was made honorary physician in 1929. He was also honorary physician to the Manor Hospital, Nuneaton, for many years. Always ready to take an active part in the local affairs of the British Medical Association, he often showed cases of clinical interest to meetings of the Coventry Division, of which he was honorary secretary in 1927–8. Besides being a member of the board of management of the Coventry and Warwickshire Hospital for many years, and chairman in 1931–2, he also served as vice-chairman of the medical committee of the hospital from 1944 to 1946, being chairman in 1946–7.

Dr. C. S. APPLEYARD writes: As one of his oldest friends and a fellow student, I would like, on behalf of my medical colleagues, to give our appreciation of the well-known "A. J.," as he was affectionately called. His services were unremitting to his hospital and to his patients. We of the profession owe him a great debt of gratitude for his kindness to and care of ourselves, our wives, and families. Himself a bachelor, he was a man of unassuming character, devoted entirely to his profession. He had been working for 16 years suffering from a painful affliction which was much graver than any of us realized. He died in harness at the age of 56 as we had always known him, the same unassuming and very gallant gentleman. His loss will be lamented by his many patients and old friends.

HARRY J. RAE, *M.C.*, M.B., D.P.H.

Dr. Harry J. Rae, who died on May 8, was until 1952 medical officer of health of the then joint public health service of the North-East of Scotland. He was 69 years of age.

Harry James Rae was born at Aberdeen on January 30, 1886, and received both his scholastic and university education in that city. He obtained the M.A. in 1907 and completed the medical curriculum, with honours, in 1911. After holding various hospital appointments and undertaking the course for the Diploma in Public Health he was appointed in 1914 to a vacancy in the school medical service of the County of Aberdeenshire. In 1915 he became the chief tuberculosis officer for that county, but shortly afterwards joined the R.A.M.C. and served in the first world war with a field ambulance unit in the Middle East. For war service he was awarded the Military Cross. On demobilization he returned to the duties of tuberculosis officer, which post he held until he became, in 1925, medical officer of health for the county. The medical officer of health of the city of Aberdeen was then the late Dr. J. Parlane Kinloch, and a partnership between city and county was established with the object of avoiding redundancy in all health service projects. Facilities available in the city health department became available for the county authority, and particularly so when legislation was anticipated and the poor law hospitals in the city of Aberdeen were taken over by the city council. When Dr. Parlane Kinloch was appointed chief medical officer in the Department of Health for Scotland in 1928,

Rae was appointed medical officer of health to the City of Aberdeen and was at the same time made head of the public health department of Aberdeen University. In view of the increased facilities which had become available the county council, in order to maintain the liaison, made an approach to the city council, and Rae was maintained in office as the county medical officer of health. In a short time a similar arrangement was made with the county council of Kincardineshire, and a joint public health service for the North-East of Scotland became a reality. It was due to Rae's untiring efforts that this project was so successful. To write reports for, and to attend the meetings of, no less than three major local authorities obviously required a man of great capacity and initiative. The pattern of the joint north-eastern public health arrangement was examined by deputations from various health authorities in other parts of Scotland and England, and many were the laudatory comments on such an arrangement.

Despite his immense amount of local authority work, Rae took a most active interest in the teaching of the undergraduates and of the postgraduates for the Diploma in Public Health. He was an active member of the Scottish branch of the Society of Medical Officers of Health and the Sanitary Association for Scotland. With the introduction of the National Health Service (Scotland) Act, 1947, the administrative control of hospitals was removed from the local authorities, but this seemed in no way to lighten the duties of the medical officer of health, though it did lessen the need for a joint public health service. In appreciation of his many years of service Rae was allowed to continue in office for a year after he was due to retire. He was appointed an Honorary Physician to King George VI in 1950, and in 1952–3 he was an Honorary Physician to the Queen. In 1953 he became a city councillor. When the British Medical Association held its Annual Meeting at Aberdeen in 1939 he served as a vice-president of the Section of Public Health and Hygiene.

He is survived by his wife, two sons, Captain Harry J. Rae, Royal Signals, and Dr. William Rae, of Aberdeen, and two daughters, Mrs. Agnes Clark, of Coupar Angus, and Dr. Isobel Margetts, of Nottingham.

H. A. MACEWEN, O.B.E., M.B., D.P.H.

Dr. H. A. Macewen, formerly a senior medical officer of the Ministry of Health, died at his home at Innellan, Argyllshire, on April 17 at the age of 74.

Hugh Allan Macewen was born on May 21, 1880, the second son of the late Sir William Macewen, F.R.S., Regius Professor of Surgery in Glasgow University, and a Past President of the British Medical Association. Hugh Macewen was educated at Glasgow Academy and at Glasgow University, where he graduated M.B., Ch.B. in 1905. In the following year he took both the Cambridge D.P.H. and the D.P.H. of the English Royal Colleges. After acting as resident medical officer at Bethesda Hospital, Hamburg, and in several Glasgow fever hospitals, he decided on a career in administrative medicine, becoming assistant medical officer of health for Stirlingshire and Dunbartonshire. A brief tenure of a similar post in Cumberland followed, and then, in 1910, he became medical officer of health for Fife and Kinross. In 1911 he was appointed medical inspector for the Local Government Board, London, and in 1920 he joined the staff of the Ministry of Health as medical officer, proceeding later in the same year to deputy senior medical officer and in 1924 to senior medical officer, a post which he filled with distinction until his retirement in 1941. During this period at the Ministry, especially prior to and during the early part of the second world war, he did very valuable and pioneer administrative work, about which an appreciative article was printed in the *Medical Officer* in 1941. From 1941 to 1942 he acted as temporary medical superintendent of Ballochyle emergency hospital, Ayrshire. During the course of his career he wrote a number of papers on public health subjects, and the first edition of his useful book on *Food Inspection* was published in 1910, the year in which he was elected a Fellow of the Royal Society of Edinburgh.

Macewen was a kindly man, rather shy and retiring, but having a courteous and friendly disposition, which made him a charming host. His home at Innellan overlooked a beautiful stretch of the Firth of Clyde, which gave him much interest and pleasure in his later years. Many people, especially the young, found him a wise counsellor. He set himself high standards and was essentially upright and extremely conscientious. In 1925 he married Dr. Barbara Cunningham, to whom he was ever devoted and whose admirable care sustained him during his last distressing illness.—H. B. K.

The death occurred at Bishop Auckland on March 4 of Dr. D. B. CAMA, who had practised in the county of Durham for many years. Dhun Boman Cama was born in Bombay on April 27, 1883, a member of a distinguished Parsee family, and received his early education in Bombay. He then studied medicine in Edinburgh, taking the Scottish triple qualification in 1911. After gaining early experience in general practice he settled at Witton Park, Co. Durham, in 1917, and in 1932 moved to Bishop Auckland, where he soon won the affection of his patients. He is survived by his widow, a daughter, and two sons. His elder son, Dr. Leonard Cama, carries on the medical practice.

J. C. writes : Strenuous work during the second world war severely affected Dr. Cama's health, but, combating ill-health with great fortitude, he continued in practice until 1951. His work exemplified the highest traditions of medical practice, and his skill, tireless efforts, and great kindness won the affection of all his patients. A man of few outside interests, he most enjoyed the company of his family and his friends, and his hospitality was renowned.

Lieutenant-Colonel H. G. L. HAYNES, who had lived and worked in Brentwood since 1920, died there on April 1, aged 77. Horace Guy Lankester Haynes was born at Evesham on June 18, 1877, and from the Grammar School there he entered Epsom College with a scholarship. From Downing College, Cambridge, where he was an exhibitioner, he went on to the Westminster Hospital, qualifying in 1903. After holding house appointments at the Westminster Hospital and the Children's Hospital, Shadwell, he was in general practice at Marksfield, Leicestershire, from 1908 until the outbreak of war in 1914. He served first in the 84th Field Ambulance and later commanded with great distinction the 2/2 London Field Ambulance, 56th Division. He was a keen Territorial and in 1932 was awarded the Territorial Decoration. Lieutenant-Colonel Haynes settled in Brentwood in 1920, where he was a prominent citizen until his death. For 25 years he was medical superintendent of Middleton Hall, a private mental home in Brentwood. During this time he not only managed the home, but was always willing to give his expert opinion and advice to the general practitioners of the town. It was during those years that he took a keen interest in the work of the British Medical Association, being president of the Essex Branch in 1926–7 and chairman of the Mid-Essex Division from 1930 to 1933. He attended a number of Annual Meetings as the representative of his Division. He also held office in

the Romford Medical Society and the Royal Medico-Psychological Association, of which he was an honorary member. During the last war he was appointed chairman of the Ministry of Labour and National Service Medical Board, and he continued to serve in that capacity until early this year.

M.R. writes: Colonel Haynes was a quiet, retiring man, difficult to know well, and slow to make friends. To those who had his friendship he was a delightful companion, full of reminiscences, with a puckish sense of humour. He was keenly interested in sport, especially rugger and cricket, and had an astounding memory for batting and bowling averages, and of famous victories and defeats of the years gone by. He was a regular habitué of Twickenham and Lord's, and enjoyed taking his friends with him and regaling them with his pungent comments on the game and his memories of the "good old days." Colonel Haynes had four sons, whose careers in medicine and the Services he watched with great pride and satisfaction. The loss of his youngest son in the Navy during the last war was a blow from which he never completely recovered. To his widow and three surviving sons his friends extend their sympathy.

Colonel ALFRED SPITTELER, who served in the Indian Medical Service for some thirty years, died at Beckington, Somerset, on April 11 at the age of 82. Born on June 10, 1872, Alfred Spitteler graduated M.B., C.M. at Madras University in 1897 before coming to London to continue his medical studies at University College Hospital. He took the D.P.H. of the English Royal Colleges in 1900 and the London Conjoint diploma five years later. Having decided to join the Indian Medical Service, he entered Netley as a probationer in March, 1900, and later in the same year was posted to India, where he served as medical officer to a number of regiments, and also as a specialist in public health. From 1902–4 he was on active service in Somaliland, being awarded the East Africa General Service medal with the Somaliland clasp. He left India for Mesopotamia early in 1915 as a member of a detachment of the Indian Expeditionary Force, and was mentioned in dispatches in the following year for distinguished service in the field. Later he served in Kurdistan, and in 1920 was again mentioned in dispatches, and in the same year he was appointed O.B.E. and promoted to lieutenant-colonel. After a further period of service in India he was for a few months in 1927 A.D.M.S. and civil administrator at Aden, being granted the brevet rank of colonel. Back in India in the following year, he retired from the I.M.S. in 1929, and came to England to settle in the West Country. For several years he was chairman of the Callington branch of the British Legion and was county commissioner for Cornwall of the Boy Scouts. During the second world war, from 1943 to 1945, he was medical officer to troops and officer commanding a camp reception station at Ilfracombe. He is survived by his widow, formerly Miss Louisa E. Dore, whom he married in 1904, and by whom he had two sons.

Mr. K. B. BELLWOOD, consulting surgeon to the ear, nose, and throat department of Bedford General Hospital, died suddenly on April 17 at his home at Bedford. He was 64 years of age. Kenneth Benson Bellwood was born at Middlesbrough on October 21, 1890, and from Sir William Turner's School, Redcar, he entered Pembroke College, Cambridge, in 1909, taking the Natural Sciences Tripos in 1912. Going on to St. Bartholomew's Hospital with a Shuter clinical scholarship, he qualified M.R.C.S., L.R.C.P. in 1914, graduating M.B., B.Chir. three years later. After qualification he held the appointment of midwifery assistant at St. Bartholomew's Hospital before entering the Royal Navy for service in the first world war. He was appointed O.B.E. in 1919 for his contribution to the war effort, and in the same year became surgeon in charge of the ear, nose, and throat department of the Royal Naval Hospital, Chatham. In the following year, on his return to civilian life, he became house-surgeon to the ear, nose, and throat department at St. Bartholomew's. In 1921 he took the F.R.C.S. and for a short time held the appointment of surgeon to the Seamen's Hospital Society at Albert Dock Hospital. Deciding to enter general practice, he went into partnership with the late Mr. W. H. Miller at Bedford, where he began to specialize as an oto-rhino-laryngologist. In 1930 he was appointed ear, nose, and throat surgeon to the Bedford County Hospital, where he built up the excellent department that exists to-day. Bellwood never spared himself, and the strain under which he worked may have influenced the course of the illness from which he eventually died. He was appointed consultant surgeon in 1948. Still in harness when his last relapse occurred a few weeks ago, he appeared to be making good progress towards recovery when he died quite suddenly and without distress. His death has saddened his many friends and old patients, who loved him for his modesty and kindness. His colleagues held him in great respect, and in 1938 he was elected president of the Bedfordshire Branch of the B.M.A. He married Miss Florence V. Cooper in 1921, and she survives him together with two daughters. A great family man, he was never happier than when surrounded by his children and grandchildren.

Dr. J. MEADMORE CROCKER, who was in practice at Bingley, Yorkshire, for over 50 years, died at the home of his daughter at Eldwick, near Bingley, on April 14, five days after his 89th birthday. James Meadmore Crocker was born at Wetherby, Yorkshire, on April 9, 1866, the eldest son of Dr. James Crocker, and studied medicine at Leeds, qualifying M.R.C.S., L.R.C.P. in 1890. He then entered into partnership with his father, who had settled at Bingley in 1871, and took over the whole of the practice when Dr. James Crocker died in 1903. After 46 years of devoted service to his patients he retired from general practice in 1936. He held many local medical appointments, including those of police surgeon, factory surgeon, public assistance medical officer, and public vaccinator. For nearly half a century he was medical officer to the Morton Banks Infectious Diseases Hospital at Keighley until he relinquished the appointment in 1948, and he had been a member of the honorary medical staff of the Bingley Hospital since its foundation in 1891. During the first world war he was in charge of the medical side of Morton Banks Hospital, with the rank of major in the R.A.M.C. He came out of retirement on the outbreak of the second world war in 1939 to take over his old practice when his successor, Dr. W. A. Lochhead, was called up for service in the R.A.M.C. There were no trams or omnibuses at Bingley when Dr. Meadmore Crocker first started in practice there, and his visits to patients were made on horseback and later in a gig, until in 1907 he became the first doctor in the town to own and drive a motor-car. He is survived by one son and one daughter.

Dr. P. C. RAIMENT, who died suddenly at Cheltenham on April 20 at the age of 74, had had an interesting career. Born on August 24, 1880, Percy Charles Raiment received his medical training at the London Hospital Medical College, qualifying M.R.C.S., L.R.C.P. in 1908. After holding the appointments of assistant house-surgeon at Huddersfield Royal Infirmary and senior house-surgeon at the East Suffolk and Ipswich Hospital, he settled in practice at Brook Green, in West London, in 1910. Becoming a member of the British Medical Association in the following year, he soon took an active part in its affairs. He was assistant honorary secretary of the Kensington Division from 1912 to 1915, and one of the representatives of the Division at the Annual Representative Meetings held at Liverpool in 1912 and at Aberdeen in 1914. The first world war, in which he served as a captain in the R.A.M.C. attached to the 6th South Lancashire Regiment, provided a dividing point in his career. Entering the R.A.M.C. from general practice, he returned to civilian life as a student once again, this time at Oxford. He entered University

College, and matriculated in 1919 at the age of 38. Two years later he obtained the B.A., with a first class in the Honours School of Natural Science, and in 1924 he proceeded to the M.A. In 1923 he was appointed senior demonstrator of biochemistry at Oxford, and in the same year he published *A Laboratory Handbook of Biochemistry*, a work written jointly with Mr. G. L. Peskett. Dr. Raiment was awarded a research scholarship by the British Medical Association in 1925–6 for work on the significance of the changes in the inorganic radicals of the blood in cases of chronic rheumatism, gout, and allied diseases, the research scholarship being renewed for 1926–7. He left England in 1928 on his appointment as professor of physiology in Cairo University, but he held the appointment for only two or three years, and on his return to England he retired from medical work.

Dr. J. F. RAMSDEN died at his home at Alverstoke, Hampshire, on May 1 after a long illness. He was 40 years of age. John Fletcher Ramsden was born on June 14, 1914, and was educated at Berkhamsted School and at Birmingham University, where he graduated M.B., Ch.B. in 1939. He then became assistant to Dr. Peter Dawes, at Feckenham, Worcestershire, but left there to serve as a surgeon-lieutenant in the R.N.V.R. during the second world war. In 1946 he became senior house-surgeon at the North Staffordshire Infirmary, Stoke-on-Trent, and in the following year joined Drs. N. L. Russell and D. C. Mackenzie in general practice at Gosport. In spite of illness in 1950, he carried on bravely for another three years, but his state of health caused him to give up work entirely in 1953. He had a most attractive personality and was beloved by his patients and by everyone with whom he came into contact. He is survived by a widow and two children, both of school age.

L. H. G. M. writes : Those of us who studied with John Ramsden in the nineteen-thirties at the Birmingham Medical School knew him to have a terrific sense of fun. Although he had great wit, he coupled this with a nature so kind and generous that he had scores of friends. On May 1 Rammy died, just short of his 41st birthday. His illness had lasted five years, and the courage he showed throughout it was seen at its best in the latter months, when his sense of humour remained unchanged and a visit to his sick-room filled one with admiration and humility. Such courage in adversity was greatness indeed. He leaves a widow and two children, to whom our deepest sympathies go in their grief.

Dr. W. NUNAN, who was well known in Bombay until his retirement from practice there in 1935, died in London on May 3 aged 75. William Nunan was born in Limerick on January 26, 1880, and was educated in Limerick and at Clongowes Wood College, Kildare. He studied medicine at Trinity College, Dublin, graduating M.B., B.Ch., B.A.O. in 1905, and proceeding to the M.D. in the following year. His brother, Sir Joseph Nunan, K.C., was at Trinity College at the same time. After some years of practice in an Irish country town Dr. Nunan went to Bombay, where he was appointed police surgeon in 1911 and coroner four years afterwards. He was also administrative medical officer of the Bombay Port Trust. Always interested in medico-legal matters, Dr. Nunan was appointed professor of medical jurisprudence and toxicology at the Grant Medical College, Bombay, in 1919, and he was an examiner in his subject to the University of Bombay. Though he led a busy life as physician and teacher, he found time to take a very active part in the life of the community, and in 1932 he was awarded the Kaisar-i-Hind medal for social and general work in India. When he returned to this country in 1935 Dr. Nunan became interested in psychiatry, and from 1946 to 1948 he worked as a psychiatric specialist in the Ministry of Pensions in Southampton and Portsmouth. Later he was appointed psychotherapist at the Tavistock Clinic. He was the author of a book entitled *Lectures in Medical Jurisprudence*, and he wrote a number of articles on psychiatric subjects, particularly on the use of suggestion as a remedial agent.

H. S. K. L. and H. G. D. write : The death of Dr. R. D. MOORE, whose obituary was printed in the *Journal* of April 30 (p. 1099), has brought to an end a life which exemplified all that was best in rural medical practice during the first part of this century. Churchdown was a small village when he settled there in 1900. Having acquired the nucleus of a practice from a doctor who had up to that time regularly visited the village from a near-by town, he was one of the first to realize the value of a motor-car to a rural practitioner. He quickly built up a practice extending over a very wide area. His stories of those pioneering days were most amusing : to stop at the foot of the Cotswolds to apply a handful of road dust to the belt drive of his car was a commonplace. He retired from practice in 1934, but continued to live in, and to take a keen interest in, the affairs of the village in which he had worked for so long. During the second world war he contrived to join the Home Guard as a combatant, again with the rank of major, and later he helped one of his former partners as medical officer to a rocket anti-aircraft battery. He remained at Churchdown until, because of failing sight, he decided to settle with his daughter and son-in-law in Kent, where he continued to make his life useful in spite of increasing blindness. During his early days he was a keen and good golfer, but cricket was the game he loved most throughout his life. He missed few county matches, and his holidays were usually found to coincide with Test matches. Few doctors can have left behind them so much affection among both patients and colleagues, an affection well earned. No effort was too great where the good of the sick was concerned, and he frequently drove patients to the hospital outpatient department in his car, remaining with them throughout the consultation to lessen their apprehension, and taking them home afterwards. His cheerfulness and constant optimism were a great inspiration to all who knew him, but his affable manner concealed a remarkable ability to recognize serious illness when he encountered it. It is still said of him that his presence alone could effect a cure, and his memory is cherished in many a home.

Mr. J. F. BALLARD, director of the Boston Medical Library, who died on May 15 aged 76, was well known to medical librarians in this country. James Francis Ballard joined the staff of the Boston Medical Library as a messenger boy in 1892 and became assistant librarian (the highest paid position in the library) in 1909. In 1927 the title of his post was changed to director. Ballard was actively interested in library affairs all his life. In 1937-8 he was president of the (American) Medical Library Association. He devised the modern classification of the Boston Medical Library (third edition, 1948) now used in a number of medical libraries throughout the world and translated into Japanese and Spanish. An authority on early medical literature, he wrote the *Catalogue of the Medieval and Renaissance Manuscripts and Incunabula in the Boston Medical Library* (Boston, 1944), a scholarly record of one of the best collections of its kind. In 1920 Ballard was sent abroad by the China Board of the Rockefeller Foundation to purchase a medical library for Peking Medical School, and on his return he was commissioned to establish a medical library for the new University of Rochester School of Medicine. At the time of his death he was consultant to several medical libraries, including the Armed Forces Medical Library, Washington. In 1942, when he had completed 50 years' service, a life-sized head-and-shoulders plaque of Ballard was unveiled in Boston Medical Library. During his service of over 62 years this medical library has grown from modest beginnings to become the third largest in the United States. James Ballard was a most genial person, who had many friends all over the world. Those who had the pleasure of meeting him at the first International Congress on Medical Librarianship in London, 1953, will be particularly sorry to learn of his passing.

Medico-Legal

FATAL REACTION TO PENICILLIN

Another death from allergic shock due to penicillin was the subject of a coroner's inquest on April 22. The case before the Westminster coroner, Dr. H. N. Stafford, was of a woman, aged 72, who was receiving penicillin treatment for furunculosis of the left hand. She had previously received several injections of penicillin, and on April 19 her medical practitioner, Dr. G. K. C. Rettie, gave her an injection of crystalline penicillin, 500,000 units, into the left deltoid muscle. About five minutes afterwards the patient became flushed and had difficulty in getting her breath. In spite of remedial measures she died within the next five minutes. Dr. Keith Simpson, consultant pathologist, carried out the post-mortem examination. He reported that a vein in the arm was transfixed during the injection, and this would result in a reaction to penicillin likely to be dangerous to life. There was no error of technique, but an unfortunate mishap. He gave the cause of death as allergic shock following penicillin injection. The coroner returned a verdict of death from misadventure.

CYANIDE POISONING OF BABY

The death of a baby from poisoning due to hydrocyanic acid gas and from dysentery was the subject of an inquest on March 1 before the Oldham Deputy Coroner, Mr. H. Armistead. According to the baby's father, Mr. A. E. Hall, the family moved house on February 25. Before moving into their new house their furniture was disinfected by the Oldham Housing Department. Among the furniture was a pram, and the baby, 9-month-old Alana Hall, was put in it at about 7 p.m. and quickly fell asleep. Later in the evening she became restless, but did not awaken. Between 9 and 10 p.m. Mr. Hall noticed that she was rather pale and had trouble with breathing. On admission soon afterwards to the Oldham Royal Infirmary she was found to be dead. During the last few days before death she had suffered from diarrhoea. After the furniture was moved into the new house, the family, with the exception of Mrs. Hall, appeared to be affected unpleasantly. Mr. Hall suffered from a severe headache, and their 2-year-old daughter was sick. The pet budgerigar died after being taken into the house.

Mrs. Hall stated that there was a small tear in the leather upholstery of the pram. The budgerigar had been in the same room as the baby.

Mr. H. Lancashire, a disinfector employed by the Oldham Corporation, said that he loaded the large removal disinfecting van with furniture, including the pram, and drove it to the Croftbank cyanide operator. After the disinfecting had been carried out he drove it to the new house and helped to unload the contents. He gave the family the usual instructions about ventilation, "getting plenty of fresh air into the house, etc." Since this case written instructions were now being left with new tenants.

Mr. N. T. Pickering, employed by the Croftbank Chemical Company as a cyanide fumigation operator, said he carried out the fumigation by the pot generation method —a mixture of 4 lb. (1.8 kg.) of water, 3 lb. (1.4 kg.) of sulphuric acid, and 2 lb. (0.9 kg.) of sodium cyanide. When fumigation was complete, he carried out the usual tests after ventilating the van. As there was plenty of breeze he did not set the fan in operation inside the van. The tests indicated that the air was clear. In answer to a question from the coroner, he said the gas could get into the pram upholstery through any tear and then come out gradually.

Post-mortem examination was carried out by Dr. C. H. Adderley, group pathologist to the Oldham Hospitals. In his opinion the cause of death was dysentery caused by *Shigella sonnei* and hydrogen cyanide poisoning. Dr. J. B. Firth, director of the North-western Forensic Science Laboratory, found traces of cyanide in the organs of the dead body, and also in the body of the budgerigar.

A verdict of accidental death was returned.

The Services

A *Supplement* to the *London Gazette* has announced the following awards:

Second Clasp to the Territorial Efficiency Decoration.—Majors F. A. Edwards, T.D., and B. L. McQuillan, T.D., R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Majors F. A. Edwards, T.D., B. L. McQuillan, T.D., and A. D. Stoker, T.D., and Captain H. W. Wykes, R.A.M.C.

Territorial Efficiency Decoration.—Majors (Honorary Lieutenant-Colonels) R. W. Fairbrother and R. B. Lumsden, Major E. Grey-Turner, M.C., Captains (Honorary Majors) C. Cockburn, C. W. A. Kimbell (retired), and N. Macmichael (retired), and Captain H. W. Wykes, R.A.M.C.

Universities and Colleges

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on January 27, with the President, Sir Russell Brain, in the chair, the following candidates, having satisfied the Censors' Board, were elected Members of the College:

J. C. Barker, M.B., A. W. Beard, B.M., W. C. Boake, M.B., H. G. T. Bridge, B.M., Stephanie J. Carter, M.B., H. D. Chalke, L.R.C.P., A. Coady, M.B., A. T. Cook, M.B., Captain, R.A.M.C., L. Cudcowitz, M.D., D. W. Davies, M.B., Pamela A. Davies, M.B., Felicity C. Edwards, B.M., M. R. E. Evans, M.B., H. A. Fleming, M.D., E. G. Galea, M.B., Mary A. Le C. Hills, M.B., W. A. Hudson, M.B., R. B. Hunter, M.B., H. K. Ibbertson, M.B., K. V. Jones, M.B., Captain, R.A.M.C., W. I. N. Kessel, M.B., J. W. Lance, M.B., I. H. Lawrence, M.B., D. W. Levy, M.B., Elizabeth A. Martin, M.B., S. Mattingly, M.B., W. K. Newton, M.B., D. W. Piper, M.B., J. C. Pond, M.B., E. J. Ross, M.B., G. F. M. Russell, M.B., M. Sandler, M.B., E. P. J. Silberstein, M.B., K. S. Somers, M.B., C. E. Stroud, M.B., G. S. Wakefield, M.B., R. T. T. Warwick, B.M., W. C. Watson, M.B., Rose A. J. Whitelaw, M.B., W. H. Wolfenden, M.B., Joan F. Zilva, M.B.

Licences

Licences to practise were conferred upon the following 71 candidates who had passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and who had complied with the by-laws of the College:

J. R. Akers, N. M. Bailey, G. C. W. Baker, Margaret A. Barrie, G. D. Blackledge, J. P. Booth, P. S. Boulter, H. J. Bradley, A. T. Brown, Elizabeth A. Burns, Enid J. Cartwright, Joan E. Chaffers, Evelyn B. Clayton, V. E. Crapnell, Hilary J. Crawford, D. R. Crockatt, Sheila R. Crosland, I. I. Dainow, D. J. Davies, J. G. Davies, Ann Davis, G. H. Daw, J. A. Dew-Jones, G. S. Dormand, L. W. S. Eyears, W. J. Fessel, Phyllis M. Fleury, J. J. Fryatt, R. H. S. Gibbs, R. C. Giles, J. N. Godlee, S. A. Greenhalgh, R. L. Hargrove, Sheila C. Hay, W. T. Henry, I. Janota, Iona Jones, P. H. Johnson, A. N. Kalra, H. W. Kirkpatrick, J. K. M. McKay, Dorothy M. Mahabir, E. Mallett, A. G. Matheson, Maryrose E. Mears, P. H. Merry, D. M. G. Murphy, G. A. Naylor, M. J. O'Neill, J. E. Pearson, Jane Platnauer, D. J. H. Prosser, Margaret A. Riddell, Muriel I. Riegelhaupt, K. P. Robinson, C. R. Salmon, A. N. Sargant, A. A. Shaikh, D. J. Sills, G. C. Spackman, J. D. Spink, F. Summers, G. G. Temple, E. R. Thomas, L. E. Thomas, D. J. Thornton, Ailsa M. Thurgar, M. D. A. Vickers, A. W. Ware, Gladys M. L. West, J. P. M. Williams.

Diplomas

Diplomas in Medical Radiodiagnosis, in Pathology, and in Tropical Medicine and Hygiene were granted, jointly with the Royal College of Surgeons of England, to the successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of December 25, 1954 (p. 1556).

Diplomas in Laryngology and Otology, in Anaesthetics, and in Ophthalmology were granted, jointly with the Royal College of Surgeons of England, to the successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England.

Other Diplomas in special subjects were granted, jointly with the Royal College of Surgeons of England, as follows:

DIPLOMA IN CHILD HEALTH.—R. S. Bull, J. A. Kay.

DIPLOMA IN INDUSTRIAL HEALTH.—A. J. Essex-Cater, W. N. Taylor.

DIPLOMA IN MEDICAL RADIOTHERAPY.—C. F. Baxter, S. Bissyllas, K. N. H. Low, Helen M. Mellor, J. W. Logan.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—V. N. Bagadia, B. C. Bignold, Maatjie V. Buhrmann, H. W. Conran, L. D. J. Coore, D. Davis, R. Doherty, T Galla, R. A. Gelfer, S. Goldin, B. Gordon, M. G. Joyasundera, A. F. Johnstone, M. H. B. Joyce, W. A. Ker, R. D. Laing, R. P. Michael, P. McK. Middleton, Marjorie A. Morgan, J. G. Neville, J. Pisani, P. K. Ray, G. H. Renton, E. A. Ritchie, D. H. Ropschitz, A. J. E. Rowe, R. Sander, C. P. Seager, R. V. Shirvaikar, H. J. Stott, J. L. Swift, L. Tarlo, J. F. Thomson, D. L. Walker, Eva Waller, J. S. Whitley, W. E. J. Wilson, E. A. M. Wood.

DIPLOMA IN PUBLIC HEALTH.—N. K. Bharucha, Nulece Cassells, Joan M. St. V. Dawkins, R. C. Greenberg, M. Husain, D. M. O. Lowry, H. R. Miller, J. P. J. O'Keefe, Hla Kyaw Pe, G. W. Piper, G. H. G. Poole, J. D. Russell, W. J. Wigfield.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on February 10 with Sir Harry Platt, President, in the chair, the Handcock Prize was awarded to P. S. Boulter (Guy's Hospital).

A Fellowship in the Faculty of Anaesthetics was granted to R. W. Milner (Jamaica).

Diplomas of Membership were granted to P. R. Holt and to the other successful candidates whose names are printed above in the report of the meeting of the Royal College of Physicians of London held on January 27 as recipients of the L.R.C.P.

A Diploma in Industrial Health was granted, jointly with the Royal College of Physicians of London, to Z. Khan; in Psychological Medicine to D. L. Walker; and in Public Health to I. H. Seppelt, in addition to the other successful candidates for these diplomas whose names are printed above in the report of the meeting of the Royal College of Physicians of London.

At a meeting of the Council of the College held on March 10, with Sir Harry Platt, President, in the chair, the second Lady Cade Medal was awarded to Squadron Leader Peter Howard; the Hallett Prize to D. Singh (Patna); the Handcock Prize was presented to P. S. Boulter (Guy's); and Paul E. Copus (Cardiff High School) was awarded the twenty-fourth Macloghlin Scholarship.

Vital Statistics

Marriages and Divorces in 1953

In England and Wales in 1953 there were 344,998 marriages, giving a rate of 15.6 persons married per 1,000 population. This rate is lower than any since 1945, when it was 18.7. London and the South-eastern region had the highest marriage rate with 16.7, and the Eastern region lowest with 13.4. On the other hand, London and the South-eastern region had the lowest birth rate with 14.1 per 1,000 population; the Northern region had the highest birth rate with 17.5. Many more marriages were celebrated in March than in any other month (56,840). The distribution of marriages is now affected largely by the date of Easter and the end of the income-tax year. The least popular month was November with 15,475 marriages. The commonest age for marriage continued to be 23 for men and 21 for women. 71 youths aged 16 were married and 1,725 girls of that age, while 248 men and 47 women aged 80 or over got married; 6 of these men were aged 90 or over. The divorce rate continued to fall, there being 29,736 divorces and 590 annulments. The commonest age group for both men and women to have their marriage dissolved was 30 to 34 years. 6,530 boys and 6,534 girls were adopted under the Adoption of Children Acts. Of the 8,787 confinements which resulted in multiple births, 8,703 were of twins, 83 of triplets, and 1 of quintuplets.—*Registrar-General's Statistical Review of England and Wales for 1953*, Tables, Part II, Civil, 1955, H.M.S.O., 5s.

Week Ending May 7

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 575, whooping-cough 1,850, diphtheria 4, measles 19,492, acute pneumonia 499, acute poliomyelitis 24, dysentery 862, paratyphoid fever 9, and typhoid fever 3.

Infectious Diseases

In England and Wales during the week ending April 30 the largest falls in the number of notifications of infectious diseases were 5,888 for measles, from 28,425 to 22,537, 174 for dysentery, from 1,053 to 879, and 148 for acute pneumonia, from 688 to 540, and the only large rise was 110 for whooping-cough, from 1,658 to 1,768.

The largest decreases in the incidence of measles were 825 in London, from 2,614 to 1,789, 791 in Essex, from 2,098 to 1,307, 733 in Yorkshire West Riding, from 3,303 to 2,570, 653 in Warwickshire, from 2,708 to 2,055, 411 in Middlesex, from 1,953 to 1,542, 374 in Surrey, from 1,345 to 971. The number of notifications of scarlet fever was 461, being 6 fewer than in the preceding week, and there were no large fluctuations in the local trends. The largest variations in the trends of whooping-cough were an increase of 30 in Kent, from 64 to 94, and a fall of 72 in Middlesex, from 146 to 74. 9 cases of diphtheria were notified, 5 fewer than in the preceding week; of these, 3 were notified in Kingston-upon-Hull C.B. and 2 in Liverpool C.B. 6 of the 15 cases of paratyphoid fever were notified in Durham (Sunderland C.B. 4).

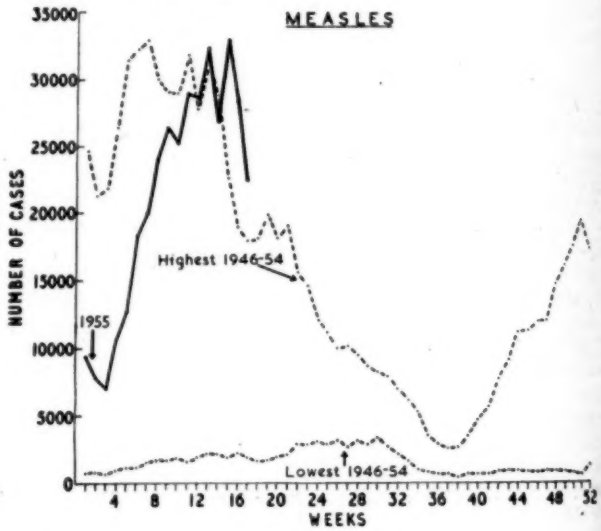
19 cases of acute poliomyelitis were notified, and these were 8 more for paralytic and 5 more for non-paralytic cases than in the preceding week. The largest returns were London 4, Kent 4, Somersetshire 3, Yorkshire West Riding 3 (Leeds C.B. 2).

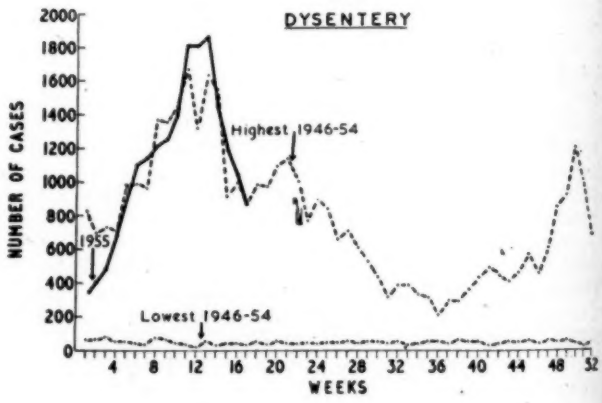
The number of notifications of dysentery fell below 1,000 for the first time for 11 weeks. The largest centres of infection were Lancashire 329 (Blackburn C.B. 45, Liverpool C.B. 45, Oldham C.B. 44, Manchester C.B. 34, Blackpool C.B. 27, Salford C.B. 25, Middleton M.B. 24, Worsley U.D. 16); Durham 110 (Easington R.D. 34, Seaham U.D. 18, Gateshead C.B. 16); London 75 (Stepney 19, Southwark 11); Yorkshire West Riding 66 (Rotherham R.D. 15, Leeds C.B. 12); Northumberland 43 (Newcastle-upon-Tyne C.B. 19); Leicestershire 37 (Leicester C.B. 27); Yorkshire North Riding 30 (Middlesbrough C.B. 30).

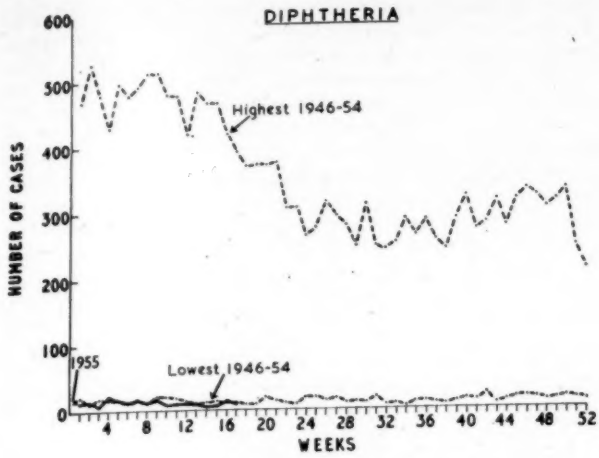
In Scotland the number of notifications of dysentery fell from 323 to 296. The largest returns were Glasgow 158 and Edinburgh 38.

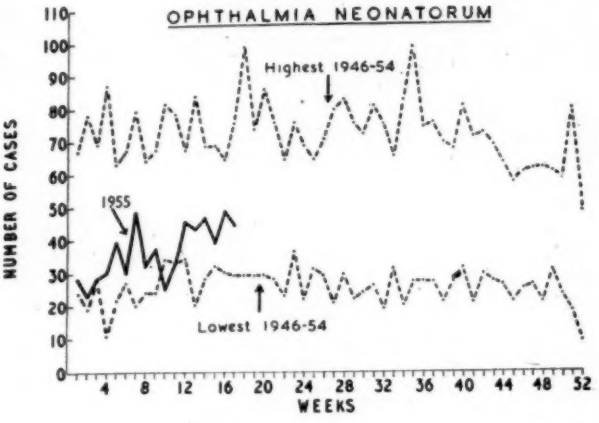
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Health of Eire in 1953

The annual report of the Department of Health of Eire for 1953–4 shows that the birth rate during 1953 was 21.1 per 1,000 of the population, being 0.8 below the rate for 1952. It was the smallest rate since 1942, but was above the rates for 1930–41. The infant mortality rate was 39 per 1,000 live births and was the lowest rate ever recorded in Eire, being 2 below the rate for 1952 and 8 below the average of the five years 1948–52. The death rate was 11.8 per 1,000 population, being 0.1 below the rate for 1952. The death rates for 1952 and 1953 were exceptionally low. The death rate varied between 12.1 and 15.3 between 1930 and 1951.

A further decline was recorded in the death rate from tuberculosis. This rate has fallen steadily from 124 per 100,000 population in 1947 to 40 in 1953, but it is still much above the level of mortality in England and Wales (20) and Scotland (26). The number of persons treated by the tuberculosis service was 36,037, a rise of 2,198 on the total for 1952. Since 1949 the number of persons treated has increased each year by 2,000–3,000. 6,602 new cases of tuberculosis came under the notice of the health authorities, a decrease of 193 compared with 1952. The deaths from infectious diseases in 1953 included 476 from influenza, 185 from gastro-enteritis (under age 2), 59 from whooping-cough, 35 from measles, 33 from poliomyelitis, 3 from scarlet fever, and 3 from diphtheria.

The cost of the local health services has risen rapidly from £5½m. in 1947–8 to over £11m. in 1953–4. During this period the proportion paid by the Exchequer has risen from 16% to 50% of the total. Grants from the Hospital Trust Fund during the year amounting to nearly £4m. were made for construction and maintenance. The sweepstakes held on the Cambridgeshire, Grand National, and Derby resulted in over £1½m. being paid to the funds of the Hospital Trust Board.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **April 30** (No. 17) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	9	0	1	0		12	0	3	0	0
Dysentery	879	75	296	18	29	759	108	280	3	3
Encephalitis, acute	3	0		0		3	2	0	0	
Enteric fever:										
Typhoid	0	0	0	0	1	3	0	1	0	0
Paratyphoid	15	0	1	0		3	1	0	0	2
Food-poisoning	177	22		2		112	13		0	
Infective enteritis or diarrhoea under 2 years				14	17				15	17
Measles*	22,537	1789	229	235	301	1,970	72	212	87	340
Meningococcal infection	38	3	18	0	2	29	6	17	0	1
Ophthalmia neonatorum	44	0	6	1		38	3	12	0	
Pneumonia†	540	27	178	6	5	521	39	144	5	1
Poliomyelitis, acute:										
Paralytic	9	2	0	0		15	2	2	0	
Non-paralytic	10	2				5	0			
Puerperal fever§	270	41	10	0		222	26	14	0	
Scarlet fever	461	28	81	37	12	623	40	136	27	39
Tuberculosis:										
Respiratory	867	85	158	30		810	107	134	30	
Non-respiratory	100	7	24	6		128	8	32	3	
Whooping-cough	1,768	115	129	46	60	2,233	88	402	29	26

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0	0	1	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0	0		0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	0	2	0	0	9	0	4	0	0
Influenza	16	0	0	0	7	10	2	1	1	0
Measles		1	0	0	0		0	0	0	1
Meningococcal infection		0	0				0	1		
Pneumonia	245	36	20	8	11	194	28	23	15	9
Poliomyelitis, acute	0	0			0	1	0	0		0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	96	17	13	2	8	87	19	14	0	7
Non-respiratory		2	2	1	1			2	1	1
Whooping-cough	0	0	0	0	0	0	0	0	1	0
Deaths 0–1 year	241	38	33	13	15	191	23	29	9	10
Deaths (excluding stillbirths)	5,729	858	613	13	202	5,270	743	702	148	189
LIVE BIRTHS	7,744	1144	1016	229	490	8,266	1229	1039	247	440
STILLBIRTHS	233	19	19			244	39	26		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

St. John "Save-a-Life" Week.—In many parts of England, Wales, and Northern Ireland May 21–28 will be the St. John Ambulance Brigade's "safe-a-life" week. During this week units of the Brigade will give life-saving demonstrations at works canteens, seaside beaches, swimming-baths, and other places of popular resort. They will be concentrating on the Holger-Nielsen method of artificial respiration. According to figures for England and Wales given by the Brigade, in 1953 1,107 persons lost their lives through accidental drowning and "nearly 1,000 more through asphyxia and electric shock." The Brigade hopes, through its "save-a-life" week, to increase the chances of recovery of those involved in such accidents. The week is being inaugurated by a meeting at the Chapter Hall, St. John's Gate, Clerkenwell, on May 21, at which the speakers will be Lieutenant-General Sir OTTO LUND and Lady MOUNTBATTEN.

Delayed Effects of Hiroshima Bomb.—Less than a year after an atomic bomb was dropped on Hiroshima in 1945, the U.S. Atomic Bomb Casualty Commission was established in Japan and began collecting data on the results of the explosion. In an interview given to the regional editor of *U.S. News and World Report* and published in that magazine on May 13, Dr. ROBERT H. HOLMES, director of the Commission, summarizes the results of what is now almost a 10-year follow-up on the inhabitants of Hiroshima. The positive findings, according to Dr. Holmes, are an increased incidence of leukaemia (103 cases) and of cataract. In addition 15 microcephalic children were born to women who were in the early stages of pregnancy at the time of the explosion, but, Dr. Holmes stresses, "no genetic effects thus far have been observed among the first generation of offspring from exposed parents." The microcephalics represented, he points out, a developmental defect *in utero*, not a genetic effect. Immediately following the dropping of the bomb, there was evidence of infertility among the survivors, "but so far as our data indicate this was a transient phenomenon, and, as the general health of the individual improved, the fertility reappeared." Dr. Holmes said that the commission were studying the possibility of premature ageing and an increased incidence of cancer, but it was too early for any definite conclusions on these questions.

Society of Chiropodists.—"One Hundred Million Feet" were referred to as the problem of the chiropodists at the annual dinner of the Society of Chiropodists at Park Lane Hotel, London, on May 13, with Mr. John H. HANBY, the president, presiding. Mr. T. T. STAMM, proposing the toast of the profession of chiropody, said that chiropodists were now united in a single body recognized by the State, and with recognized standards of training and ethics. Having attained this position it must now be their purpose to develop it in the public interest. Chiropody's function was not just to provide comfort but to improve function and keep feet on the road. The chiropodist was an essential member of the orthopaedic team. Mr. Stamm summed up by saying that the profession of chiropody should now have three main aims: to work to restore foot function, to retain its independence, and to increase its contact with the medical profession. Mr. HANBY, replying to the toast, stressed particularly the chiropodist's role in prevention among schoolchildren and, at the other end of the scale, in making the aged mobile. The latter was an urgent problem, and, as to the former, there were too few chiropodists in the school health service. Mr. J. R. HALL proposed the toast of the guests, on behalf of whom Dr. W. S. C. COPEMAN replied.

Harveian Society of London.—The legal profession was well represented at the Buckston-Browne–Gray-Hill dinner, held on May 13 at the Royal College of Surgeons. Sir FRED PRITCHARD, Q.C., proposing the toast to the Harveian Society of London, spoke of the value of friendships formed through intercommunication of two great professions. Some much-needed reforms to-day could come about only if the law and medicine worked together to secure them, with the object of common service in mind. Nearly everybody agreed that the rules which affect present-day laws about insanity should be overhauled. Neither profession could revise the rules alone, but the law and medicine together should see to it that the rules were revised in a way which would be of advantage to the community. Responding to the toast, Mr. A. DICKSON WRIGHT, the president of the Harveian Society, supported the idea that the law and medicine should collaborate more closely, and mingled humorous and serious remarks about both professions in a way entirely his own. The health of the guests was proposed by Dr. D. GERAINT JAMES, and Mr. H. EDMUND DAVIES, Q.C., Recorder of Cardiff, replied.

Eighth World Health Assembly.—At the opening session on May 10, Dr. IGNACIO MORONES PRIETO, Mexico's Minister of Health and Welfare, was elected president of the Assembly. Dr. S. AL WAHBI (Iraq), Dr. J. GRATZER (Austria), and Sir ARCOT MUDALIAR (India) were elected vice-presidents.

U.S.A. Poliomyelitis Inoculation Programme.—On May 13 the U.S. Public Health Service cleared over four million doses of Salk poliomyelitis vaccine, and inoculation in the United States has been resumed. Meanwhile President Eisenhower has accepted the Department of Health and Welfare's recommendation that distribution of the vaccine should continue on a voluntary basis. While there is a shortage of vaccine, inoculation will be limited to children between the ages of 5 and 9. A report from Denver, Colorado, states that the parents of two unrelated children who had been inoculated with Cutter vaccine have developed paralytic poliomyelitis. Dr. FLORIO, the city health director, is quoted as saying: "It is definitely possible that these parents contracted polio from their children."

Sex Hormones.—Last autumn representatives of the B.M.A., the Pharmaceutical Society, and the Royal College of Nursing discussed the dangers inherent in the general availability of sex hormones without prescription and what measures of control were needed. As a result of these discussions the following statement was issued by the council of the Pharmaceutical Society and published in a recent issue of the *Pharmaceutical Journal* (April 16, p. 288):

> Some time ago in view of reports of the misuse of sex hormones for the suppression of lactation and the treatment of menopausal conditions the British Medical Association approached the Society to discuss whether any control should be imposed on their distribution and enquiry was made as to the practice of pharmacists in response to requests for such products. This showed the need for some regulation of the supply of sex hormones and after consideration it was agreed that the appropriate course would be for the matter to be the subject of advice to pharmacists by the Council of the Society. Accordingly the Council have decided to advise pharmacists not to supply sex hormones or their preparations unless satisfied that the customer is obtaining them on medical advice. This does not apply to cosmetic preparations containing hormones which are at present the subject of separate consideration.

American Grants for Leukaemia Research.—The Robert Roesler de Villiers Foundation (of New York) will shortly make grants-in-aid in support of research on leukaemia. Investigators in the United Kingdom who are interested should apply to the Regius Professor of Physic, University Department of Medicine, Tennis Court Road, Cambridge, before June 15. During the year 1955, awards of not more than $1,000 (about £350) will be made to any one research worker.

Medical Candidates.—The names of two other medical candidates for Parliament have been announced, in addition to those mentioned in the *Journal* of May 7 (p. 1149) and May 14 (p. 1230). They are: WILLIAM STANLEY RUSSELL

THOMAS, Brecon and Radnor, Liberal (1919). Barrister-at-law, Lincoln's Inn. M.P. for Southampton from 1940 to 1945. Deputy Chairman, London Liberal National Party, 1937–45. Member, Select Committee on Public Petitions, 1942–4. Member, Select Committee on National Expenditure, 1944. JESSE DICKSON MABON, Renfrewshire West, Labour and Co-operative (1954).

Sir James Learmonth, Regius Professor of Clinical Surgery at Edinburgh, is visiting Strasbourg University from May 21 to 25 under the Foreign University Exchange Scheme.

COMING EVENTS

Polish Medical Association in Great Britain.—Annual meeting on May 28 and 29 at 18, Queen's Gate Terrace, London, S.W.7. Dr. J. CZEKALOWSKI will speak on "The Newer Approach to the Virus Problem." Full details of programme from hon. secretary, Polish Medical Association, 14, Collingham Gardens, London, S.W.5.

Concert in Aid of Lord Horder Centres for Arthritics.—IRENE KOHLER and the London Philharmonic Orchestra at the Royal Albert Hall on June 2 at 8 p.m. Programme and tickets (21s. to 2s.) from the Hall or the usual agents.

NEW ISSUES

British Journal of Ophthalmology.—The new issue (Vol. 39, No. 5) is now available. The contents include:

GENERALIZED CHOROIDAL SCLEROSIS. COURSE AND MODE OF INHERITANCE. Arnold Sorsby and J. B. Davey.
OCULAR CHANGES IN THE BLOCH-SULZBERGER SYNDROME (INCONTINENTIA PIGMENTI). J. Graham Scott, A. I. Friedmann, M. Chitters, and W. J. Pepler.
PRELIMINARY REPORT ON THE USE OF CONTRAST MEDIA IN ORBITAL RADIOGRAPHY. J. W. Cowie and J. S. Groves.
VARIATION OF FIXATION DIRECTION WITH COLOUR OF FIXATION TARGET. D. H. Fender.
CLASSIFICATION OF ANGIOID STREAKS. R. J. McWilliam.
OPHTHALMIA NODOSA DUE TO CATERPILLAR HAIRS. J. A. Corkey.
DIBENZYLINE IN GLAUCOMA. John Primrose.
ABNORMAL FUNDUS REFLEXES AND RETINITIS PIGMENTOSA. R. P. Crick.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Archives of Disease in Childhood.—The new issue (Vol. 30, No. 150) is now available. The contents include:

ON THE PROGNOSIS OF CRETINISM. David Lawson.
THE ABSORPTION OF SHORT-CHAIN FATS BY PREMATURE INFANTS. Selma E. Snyderman, Soledad Morales, and L. Emmett Holt, jun.
A STUDY OF CEREBRAL PALSY IN THE CHILDHOOD POPULATION OF EDINBURGH. T. T. S. Ingram.
CONGENITAL PNEUMONIA AND PNEUMONIA IN THE NEONATAL PERIOD. Kr. Harnaes and K. H. Torp.
HAEMOGLOBIN AND RED CELLS IN THE HUMAN FOETUS: II. THE RED CELLS. Elizabeth P. N. Turnbull and James Walker.
HAEMOGLOBIN AND RED CELLS IN THE HUMAN FOETUS: III. FOETAL AND ADULT HAEMOGLOBIN. Elizabeth P. N. Turnbull and James Walker.
BLOOD FORMATION IN INFANCY: PART III, CORD BLOOD. John Marks, Douglas Gairdner, and Janet D. Roscoe.
THE USE OF COBALT IN SOME COMMON ANAEMIAS OF CHILDHOOD. B. L. Coles.
THE DETERMINATION OF BLOOD PRESSURE IN INFANTS BY THE FLUSH METHOD. John Reinhold and Michael Pym.
CIRCULATING BASOPHILIC LEUCOCYTE COUNTS IN THE NEWBORN. Ross G. Mitchell.
THE EVALUATION OF THE EOSINOPENIC RESPONSE TO CORTICOTROPHIN AND CORTISONE IN THE NEWBORN INFANT. James W. Farquhar.
THE EFFECT OF DISEASE AND INJURY ON THE ADRENAL CORTEX OF STILLBORN AND NEWBORN INFANTS. F. A. Langley and J. C. Burne.
A CASE OF GALACTOSAEMIA WITH SPECIAL REFERENCE TO MENTAL DEVELOPMENT. P. R. Clay and C. T. Potter.
THE AMINO-ACIDURIA IN GALACTOSAEMIA. D. C. Cusworth, C. E. Dent, and F. V. Flynn.
A STUDY OF THE GENETICS OF GALACTOSAEMIA. A. Holzel and G. M. Komrower.
A FAMILIAL TUBULAR ABSORPTION DEFECT OF GLUCOSE AND AMINO-ACIDS. Joseph Luder and Wilfrid Sheldon.
A CASE OF HYPOTHYROIDISM WITH NEPHROCALCINOSIS. Jean M. Naylor.
METASTATIC TUBERCULOUS ABSCESSES. F. J. W. Miller and Maureen Cashman.
BILE PERITONITIS IN INFANCY. Pamela A. Davies and A. Elliot-Smith.
SUPERFICIAL GANGRENE OF THE SKIN IN CHICKENPOX. R. S. Illingworth and R. B. Zachary.
SUBACUTE AND CHRONIC INTUSSUSCEPTION IN INFANTS AND CHILDREN. Duncan Macaulay and Thomas Moore.
GANGRENE OF THE EXTREMITIES IN TWO AFRICAN INFANTS. Lorna G. Macdougall.
A CASE OF FIBROMA OF THE LEFT VENTRICLE IN A CHILD OF 4 YEARS. Ursula James and Margaret H. Stanfield.
FAMILY PERIODIC PARALYSIS IN A MENTALLY DEFECTIVE BOY. Thomas A. Couston.
PELLAGRA IN AN ENGLISH CHILD. G. W. Hickish.

Issued six times a year; annual subscription £3 3s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, May 23

BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At Middlesex Hospital Medical School, 8 p.m., Mr. Philip Wiles: Athletic Injuries as Seen in the Hospital.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in pathology by Dr. R. J. Huebner (Bethesda, U.S.A.): Newly Recognized Respiratory Viruses and the Search for Diseases which they Cause.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. A. C. Corcoran (Cleveland): Current Developments in Hypertension.

Tuesday, May 24

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. W. N. Goldsmith: Skin Lesions in Metabolic Disorders.
LONDON AMATEUR BOXING ASSOCIATION.—At 69, Victoria Street, S.W., 8 p.m., Mr. A. Rugg-Gunn: Eye Injuries.
NATIONAL BOOK LEAGUE.—At 7, Albemarle Street, W., 7.30 p.m., Professor J. Z. Young, F.R.S.: Memory.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor H. G. Hanley: Surgery of Male Subfertility.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Physiology Lecture Theatre, 5 p.m., Dr. A. C. Corcoran (Cleveland Clinic, Ohio): Evaluation of Antihypertensive Drugs.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, W.C., 5.15 p.m., Cushny Memorial Lecture by Professor R. A. McCance, F.R.S.: Metabolism and Renal Function in the First Few Days of Life.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY.—5 p.m., Almroth Wright Lecture by Lord Stamp: Action of Bacterial Enzymes on Immunizing Antigens.

Wednesday, May 25

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Dr. J. D. Sutherland: Psychotherapeutic Provisions in a National Health Service.
EUGENICS SOCIETY.—At Royal Society, Burlington House, 5.30 p.m., Dr. J. A. H. Waterhouse, Ph.D.: Twins and Genetics.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Localized Diseases of the Collagen.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. J. Anderson: General Aspects of Erythroblastosis and its Impact on Pathological Processes.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Professor T. N. A. Jeffcoate: Pruritus Vulvae.

Thursday, May 26

EDINBURGH UNIVERSITY.—At West Lecture Theatre, University New Buildings, 5 p.m., Dr. D. J. Guthrie: The Hippocratic Tradition.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Blood Coagulation.
MANCHESTER UNIVERSITY.—At the Medical School, 4.30 p.m., annual Wood Jones Commemoration Lecture by Professor John Morley: How to Become a Surgeon.
NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Professor J. Trueta: Reflections on Bone Growth after Eight Years' Study.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. E. Clarke: Epilepsy, Recent Advances.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Arnott Demonstration by Dr H. Stansfield: The Visual Pathway.
ROYAL NORTHERN HOSPITAL.—2.30 p.m., Dr. C. Foster Cooper: Day-to-day Diabetic Difficulties.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Medical School, Small's Wynd, Dundee, 5 p.m., Mr. A. Dickson Wright: Sciatica of the Arm.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., postgraduate demonstration in psychiatry.

Friday, May 27

CAMBRIDGE MEDICAL SOCIETY.—At Addenbrooke's Hospital, 3 p.m., Dr. Joan G. Malleson: Disorders of the Menopause and their Treatment.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. R. Bignall.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. J. G. Yates-Bell: Treatment of Hydronephrosis.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, W.C., 5.15 p.m., Cushny Memorial Lecture by Professor M. L. Rosenheim: Functional Aspects of Renal Failure.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Kustow.—On May 10, 1955, at Queen Charlotte's Hospital, London, W., to Ann (formerly Justus), wife of Dr. Bernard Kustow, a son—Alexander Daniel.
Quantrill.—On May 7, 1955, at Peel Street Hospital, Nottingham, to Edna, wife of Dr. Douglas W. Quantrill, a daughter.

DEATHS

Molesworth.—On April 10, 1955, at Priory Lodge, St. Margaret's Bay, Kent, Theodore Henderson Molesworth, M.B., F.R.C.S., aged 82.
Reichenfeld.—On April 16, 1955, at Birmingham, Isidore Ernst Reichenfeld, M.D., aged 62.
Rodgers.—On March 24, 1955, at "Clayton," 115, Cowden Drive, Bexhill-on-Sea, Sussex, Frederick Millar Rodgers, O.B.E., M.D., D.P.H.
Scott.—On March 22, 1955, at his home, The Briars, 346, Loose Road, Maidstone, Kent, David Scott, M.R.C.S., L.R.C.P., late of Leyton, London, E., aged 87.
Spitteler.—On April 11, 1955, Alfred Spitteler, O.B.E., M.R.C.S., L.R.C.P., D.P.H., Colonel, I.M.S., retired.
Wilson.—On April 16, 1955, at his home, 8, Milnthorpe Road, Eastbourne, Sussex, Thomas Wilson, F.R.C.S.I., formerly of 108, Chevening Road, London, N.W., aged 89.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Deposit of Tartar on Dentures

Q.—*Could you please advise on the cause and removal of a deposit on my dentures which resists the commercial cleaning solutions? It forms a minute, spreading, fawnish-white coating over the plastic of the dentures, especially in the interstices of the teeth. If I retain the dentures in my mouth overnight for three or four nights the deposit at once gets the upper hand. If the deposit is "tartar," what is tartar? Where does it come from? What is the best way to prevent its deposition? Does its appearance depend on the pH of one's saliva? Will anything dissolve it from the dentures?*

A.—The deposit on the dentures is probably "tartar." The mode of deposition of this tartar or calculus is still undetermined, though much work has been done on it. The saliva contains a very high concentration of calcium and phosphorus, and their stability may depend on the colloids also present in the saliva. It has been postulated that the low tension of carbon dioxide in the mouth, with consequent loss of carbon dioxide from the saliva, causes precipitation of calcium salts. It is thought that the presence of carbon dioxide is important in maintaining a high concentration of calcium salts in the saliva. The *p*H of the saliva is very variable, largely depending on the carbon dioxide content, and there is no obvious correlation of figures for salivary *p*H and tartar deposition from one individual to another.

The tartar deposit tends to be greatest opposite the openings of the salivary ducts, and forms on the natural teeth and to some extent on dentures. There is at present no known way of stopping this deposition and recourse must be had to its physical removal. Brushing the dentures each day with a soft brush and soap should keep them well polished and free of tartar, but if the surface of the dentures loses its polish tartar deposits may be more marked. It would be as well, if the deposit continues, to get the dentures repolished, as this helps to prevent further deposition.

Serology in Herpes Zoster

Q.—*What is the present status of the complement fixation test performed on the patient's serum in the diagnosis of herpes zoster? Has any other diagnostic test been designed for this purpose? Have any of these tests been carried out on a series of normal individuals? Has it definitely been established that herpes zoster is due to a virus? What is the evidence for this? Please give references.*

A.—Serological tests for herpes zoster are difficult to perform because the antigen used in the test consists of vesicle fluid collected from cases of varicella or zoster during the early stages of the eruption. The limitations of such a test are considerable. However, a number of investigations carried out some years ago indicated that the serum from patients convalescent from zoster fixed complement in the presence of zoster or varicella vesicle fluid antigen.[1] In one or two cases increases in antibody titre were detected. Furthermore, these serological tests indicated a very close relationship between the two viruses. The sera from normal individuals usually have a lower antibody titre or are clearly negative, but the findings in both cases must be related to the titre after the onset of infection.[1]

The great difficulty about varicella and zoster viruses is that they cannot be grown in the ordinary culture media used in virology. But recently Weller has managed to propagate both viruses in tissue culture.[2,3] This development may lead to the production of a diagnostic antigen. Another test of some practicable value is the examination of scrapings from vesicular lesions for the presence of multinucleate epithelial cells and intranuclear inclusion bodies. These cytological changes are commonly found in both zoster and varicella, but they cannot be distinguished one from the other nor from similar lesions seen in herpes simplex infections. However, herpes simplex virus can be grown quite readily in the laboratory, which helps to distinguish the two if the need arises.

The virus aetiology of zoster is based on two main findings. The disease has been reproduced in human beings by direct inoculation of vesicle fluid.[4] In some cases typical varicella has resulted (usually in children) or a local vesicle has developed. Natural cases of varicella in children resulting from an adult with zoster are well recognized.[5] Secondly, the virus has been grown in tissue culture from vesicle fluid, and the actual causative agent, the virus elementary bodies, has been seen in vesicle fluid under the electron microscope.[6]

REFERENCES

1 Brain, R. T. (1933). *Brit. J. exp. Path.*, **14**, 67.
2 Weller, T. H., and Stoddard, M. B. (1952). *J. Immunol.*, **68**, 311.
3 —— (1953). *Proc. Soc. exp. Biol. (N.Y.)*, **83**, 340.
4 Kundratitz, K. (1925). *Z. Kinderheilk.*, **39**, 379.
5 Blank, H. (1949). *Acta derm. venereol.*, **29**, 77.
6 Rake, G., Blank, H., Coriell, L. L., Nagler, F. P. O., and Scott, T. F. McNair (1948). *J. Bact.*, **56**, 293.

Ultrasonic Vibrations and Gall-stones

Q.—*I have heard that it is possible to disintegrate gall-stones in situ by directing ultrasonic waves on them. Has this therapy in fact been used with any success?*

A.—A number of physical studies have been made in the attempt to disintegrate calculi, both urinary and biliary, by ultrasonic vibrations. The results have been discussed by Mulvaney.[1] Up to the present only partial disruption of the calculi has been achieved and that only under conditions which are quite impracticable clinically. Even if disintegration of gall-stones in the gall-bladder could be achieved clinically, it would seem inadvisable to carry this out, as the small fragments resulting would be more of a danger to the patient than the larger gall-stones from which they are derived, owing to the likelihood of their passing into and obstructing the common bile duct.

REFERENCE

1 *J. Urol.*, 1953, **70**, 704.

Psychiatric Treatment of Adult Enuretic

Q.—*What can psychiatric treatment offer a man of 26 who is a persistent bed-wetter, and has on that account ruled out the possibility of marriage?*

A.—It is improbable at this age that enuresis is the result of a primary emotional disturbance. In children the opposite is the case, but those with emotional problems tend to get better with time or with treatment, leaving a residue of cases where the cause is constitutional and biological rather than psychological. It is likely that the patient belongs to this group, and inquiry should be made about the depth of his sleep, for if he sleeps very heavily dextro-amphetamine taken at bedtime may result in his being awakened in time by the discomfort in his bladder. The dose required may vary from 2½ to 30 mg. If there is a history of precipitancy of micturition by day, he should be tried on propantheline bromide ("probanthine") 15 mg. at bedtime. Nocturnal epilepsy is less likely as a cause, but inquiry should be made about disturbance of his bedding, biting of his tongue, and whether attacks have occurred by day.

Although it would be unwise to promise it, it is nevertheless true that some of these patients are cured by marriage. The most probable explanation lies in their being disturbed during the night by the movement of the other occupant of the bed. This, added to bladder discomfort, may be sufficient to awaken the deep sleeper.

There may of course be an emotional reaction which is secondary to the enuresis but which requires treatment. If the patient has ruled out marriage as a possibility, it

sounds as if this may be the case. Enuretics often marry, and women will frequently accept the burden involved with patience. Psychotherapy in such a case would not affect the enuresis, but might encourage a more hopeful and resolute acceptance of the disability. Such psychotherapy should be on the level of discussion and counselling, and extensive procedures should not be required.

Sensitization to Streptomycin

Q.—*In the case of a person who is administering streptomycin by injection and has become sensitized to the drug, as evidenced by dermatitis of the hands, is there any likelihood of this sensitization disappearing spontaneously while contact with the drug is maintained? Full protective technique is observed, and it is presumed that the absorption of the drug occurs by inhalation.*

A.—In our experience sensitization to streptomycin, acquired by handling the drug, does not disappear spontaneously while contact with the drug is maintained. If the patient ceases contact with the drug, the dermatitis may clear up, but fresh contact is apt to result in a fresh outbreak. Of course, it must be determined that the sensitization is indeed to streptomycin. The simplest technique for determining this is to inject 25 to 100 micrograms in 0.1 ml. intradermally. If the patient is sensitive erythema appears, which may be observed at 6, 12, or 24 hours after the injection. The actual dose given should depend on the severity of the symptoms. The higher dose may produce some general exacerbation if the patient is very sensitive, but the test should not be regarded as negative unless the full dose of 100 micrograms has been given. Desensitization is feasible although a little tedious. The technique is described by Crofton.[1] Clinical details and the frequency of this form of sensitization have been described by the Ministry of Health[2] and by Crofton and Foreman.[3]

REFERENCES

1 *British Medical Journal*, 1953, **2**, 1014.
2 Ibid., 1953, **2**, 39.
3 Ibid., 1948, **2**, 71.

Olfactory Hallucinations

Q.—*A close relative of mine, aged 28, complains that her clothes emit obnoxious odours due to some naphthalene which was once used in her clothes cupboards. The cupboards have since been cleaned to her satisfaction, but she still complains that people in buses, theatres, and shops can still smell her clothes, even at a distance. She is convinced that when people smoke or sniff they do so because of her, and as a result is loath to go out. Neither I nor anyone else can smell anything abnormal. Could this condition be due to any nasal or other physical condition, or should she be referred for a psychiatric opinion? The patient is the neatest of persons and fastidious to a degree. What treatment is advised?*

A.—This patient should certainly be referred for a psychiatric opinion. The symptoms described could not be solely due to any nasal or other physical condition, since she undoubtedly seems to misinterpret the behaviour of others. It is all very suggestive of the onset of schizophrenia. The first thing, however, would be to have a competent psychiatric opinion before deciding what treatment should be adopted. To suffer from olfactory hallucinations, coupled with other misinterpretations, at the age of 28 is unlikely to be due to a depression, although such symptoms can occur in involutional melancholia, nor are any other symptoms of depression described in this case.

Treatment of Warts

Q.—*I would be grateful if you would tell me what you consider the best treatment for warts.*

A.—Treatment of infective warts may be radical, and this is indicated when they are single or few and in sites where they are for one reason or another troublesome. The best radical measure is careful curettage under local analgesia, the wart being shelled out and the cavity being swabbed with phenol or trichloracetic acid. Cautery, diathermy, caustics, freezing, and radiotherapy are used to the same end but are more crude, lack the precision of curettage, and are not without dangers.

The oedematous warts occurring at the anus, and on the vulva or prepuce, may be associated with local discharges. Effective treatment of the discharge will usually clear the warts. Otherwise they are commonly responsive to a single or repeated painting of podophyllin resin (25% in 90% spirit).

Multiple plantar warts and mosaic warts often clear after soaking the part in 3% formalin for ten minutes at night for six weeks. In general, desiccating measures which cause some desquamation of the skin and antiseptics have some value, as for instance sulphur and resorcin pastes for flat warts, but most other treatments are probably effective only through suggestion. Wart charming is an effective remedy in the hands of the few.

Nervous instability with sweating and greasiness of the skin predisposes to warts and their spread, and this probably accounts for their high incidence in children. The manner in which remedies are prescribed and presented is important. For the great variety of measures employed in this field the reader may consult textbooks.

Toxicity of Rotenone

Q.—*I should be grateful for information on the chances of dermatitis or toxic effects in a factory where girls are engaged in packing an insecticide containing 0.5% powdered rotenone. The percentage has recently been raised from 0.25%. No physical ill effects have ever been found with the latter concentration, but there is, of course, some escape of the powder into the air. The methods adopted to prevent any ill effects consist in the use of an industrial vacuum cleaner and the provision of light fabric face masks.*

A.—Rotenone is the active principle of derris root and also of various tropical plants of the genus *Lonchocarpus*. Information about derris root can be obtained in the earlier editions of the *British Pharmaceutical Codex*, but not in the 1954 edition. References to rotenone are to be found in *Occupational Diseases of the Skin* (2nd edition) by Schwarz, Tulipan, and Peck, pp. 413–14. A paper by Haag[1] deals with toxicological studies of *Derris Elliptica*. It is said that derris dust if inhaled in sufficient quantity will produce fatty degeneration of the liver. Rotenone is a sensitizer, and dermatitis has been reported amongst workers who make and use spray solution containing it.

It would be useful to know the other ingredients of the powder containing 0.5% rotenone. Some of the so-called "inert" powders which have been used as vehicles, such as kaolin and talc, are known to produce pulmonary fibrosis.

Packing of powders is commonly done under exhaust ventilation, and if this is efficient there should be no need for the workers to wear respirators.

REFERENCE

1 *J. Pharmacol.*, 1931, **43**, 193.

Treatment of Uterine Hypoplasia

Q.—*What is the treatment of sterility due to uterine hypoplasia?*

A.—Uterine hypoplasia is frequently diagnosed as a result of an impression gained during bimanual examination, and this is unreliable evidence no matter how skilled the observer. As a rule the diagnosis requires examination under anaesthesia, measurement of the uterus, and diagnostic curettage. To justify a diagnosis of uterine hypoplasia, the overall length of the uterus should be 2½ in. (6.3 cm.) or less, and the endometrium should be thin and should show an unstimulated appearance on microscopic examination. The uterine index—that is, the length of the cavity of the body of the uterus relative to the length of the cervical canal—is difficult to measure accurately, and, in any case, is not so informative as was once believed. Uterine hypoplasia is usually manifested by a late menarche, although this symptom by itself is of little significance.

Amenorrhoea or infrequent menstruation is also to be expected; a scanty regular loss is not necessarily indicative of hypoplasia.

However, even if uterine hypoplasia is proved to exist, there is no evidence that the condition *per se* lowers fertility, despite the general statements to the contrary which are found in most gynaecological textbooks and in monographs on infertility. Why should it? A small cavity with ill-prepared walls does not prevent conception, as the frequent occurrence of tubal pregnancy proves. It might, however, favour abortion. The only circumstance in which uterine hypoplasia is *associated* with infertility is when it is the result of inadequate ovarian function. In such case the uterus can be made to grow to normal size with oestrogen, but this does not raise fertility and the effect is only temporary. For the real cause of the sterility is failure of the ovary to produce ova, so treatment should be directed to the establishment of ovulation, even though the results are generally unsatisfactory. If uterine hypoplasia occurs despite normal ovarian function, then it is presumably because the uterus is unresponsive to ovarian hormones. It is the target organ which is at fault, the fault being unknown but allegedly inherent. In that case treatment with oestrogens is not likely to affect the uterus at all.

A critical, some may say hypercritical, outlook leads to the conclusion that uterine hypoplasia is more often a convenient label than a proved state; and that when it is present its treatment is either unnecessary or is doomed to failure unless its cause can be traced and corrected.

Methylpentynol in Pregnancy

Q.—*I should be glad to know whether there is any danger in expectant mothers taking methylpentynol before visiting the dentist, especially when they are going to have gas.*

A.—There are no reports in the literature to suggest that methylpentynol is dangerous for expectant mothers. It is destroyed in the body very much like ordinary alcohol, and the ill effects of too much methylpentynol resemble the effects of too much alcohol.

Treatment of Bee Stings

Q.—*What is the best treatment for bee stings? I am a member of a bee club and have been asked for advice.*

A.—Bee stings may result in a local reaction due to the injected bee-venom, a more generalized allergic reaction, or both.

The sting should be gently removed. Local therapy consists in the application of an antihistaminic ointment: various alkali solutions are also of help—for example, soap, sodium bicarbonate, methylene blue, weak ammonia, or calamine. For the milder urticarial reactions an antihistaminic drug, preferably one that does not cause drowsiness, ephedrine, or a combination of these two should be given. For the severe allergic reactions, angioneurotic oedema, severe dyspnoea, collapse, or unconsciousness, 1:1,000 adrenaline should be given in doses of 5–10 min. (0.3–0.6 ml.) and repeated as necessary. Some sensitized bee-keepers have found taking a small dose of ephedrine prior to handling the bees a means of reducing the severity of their reactions. All might well be advised to carry with them ephedrine and an antihistaminic to take as soon as they are stung, while the more severely affected should carry isoprenaline.

"Desensitization" or hyposensitization presents a series of difficult problems which are well discussed by Mueller and Hill, of Boston.[1] Isolated successful cases have been recorded, but it is not known for a series of patients what proportion would be adequately protected nor for how long the protection is likely to last once the injections are stopped. Bee-venom antigen is available from commercial firms, but skin testing and hyposensitization should be advised and carried out by an expert, for the antigen is a potent one. As in the treatment of hay fever, the dosage depends on the degree of sensitivity and even in skilled hands carries some risk of untoward reactions occurring. One might expect the results to be similar to those of hyposensitization to hay fever and other immediate wealing allergies. The writer hesitates to advise hyposensitization except in individual cases and only when undertaken by experts.

REFERENCE

1 Mueller, H. L., and Hill, L. W. (1953). *New Engl. J. Med.*, 249, 726.

Sparks from a Silk Shirt

Q.—*When I wear a leather corset and an artificial silk shirt the crepitations and sparks of static electricity are observed on removal of the shirt. Are such sparks sufficient to ignite ether or petrol?*

A.—The only safe answer is yes, though the risk of ignition of dangerous vapours by the crepitations and sparks alone is probably small and would require the co-existence of various other favourable factors. Nevertheless, in these kind of circumstances no avoidable risk, however slight, should ever be incurred. The conditions described in the question are particularly favourable to the development of static charges of high potential.

It has long been known that the ordinary movements of an anaesthetist, or other person in an operating theatre, can build up in himself a high charge of static electricity. Should he then approach or handle an object of lesser electric potential a spark will be formed sufficient to ignite or explode any dangerous vapour in the vicinity. This is known to be the explanation of many disasters that have occurred. If ordinary movements can do this, how much more so will the relatively violent ones described in the question? Silk is considered to be specially dangerous, and other fabrics may be little less dangerous. The risk of such accidents is much accentuated by the use of footgear made of ordinary non-conductive rubber or other similar material and also by furnishing operating rooms with non-conducting floor coverings such as linoleum.

Specific Desensitization to Foods

Q.—*An asthmatic child has been advised to avoid milk, fish, eggs, cheese, chocolate, and nuts. As it will be difficult to provide such a diet, can you please advise me whether it would be worth undertaking specific desensitization, and, if so, how should it be done?*

A.—Specific desensitization to foods is not advised. Neither oral nor parenteral "hyposensitization" have been proved to be effective, and both methods are considered by most authorities to be ineffective. Complete elimination from the diet and re-testing by ingestion every six months or so is the accepted treatment of proved food allergies.

The writer, however, would emphasize the great importance of not eliminating from the diet of any asthmatic (child or adult) any food unless it has been shown beyond doubt that its ingestion, even when introduced into the diet in a hidden or unsuspected form, repeatedly precipitates asthma.

Correction.—In the Parliamentary report on the consumption of welfare foods (*Journal*, May 14, p. 1228) the word "tons" (of dried milk) should read "tins."

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